Smoking, Personality and Stress as Risk Factors for Cancer and Coronary Heart Disease.

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SUMMARY

It is often suggested that the incidence of cancer and coronary heart disease could be much reduced or even eliminated if only people ceased to smoke cigarettes and reduced their cholesterol level through appropriate eating. The evidence suggests that such views are unrealistic, and that cancer and CHD are the product of many risk factors acting synergistically. Psychosocial factors (stress, personality) are about six times as predictive as smoking, cholesterol level, and blood pressure, and have proved to be much more accessible to prophylactic treatment. There is no such evidence concerning quitting smoking, which at best has only minimal effects on future health.

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(1) Introduction:

Debate concerning the effects of smoking on health.

Laymen and medical professionals alike often ask questions regarding the causation of cancer and coronary heart disease, the two major killers in our present-day civilization, expecting a simple answer like "Smoking causes cancer and coronary heart disease". Or cholesterol, produced by an unwise diet, may be blamed. It need hardly be argued that to look for single causes for complex phenomena is not a meaningful occupation, particularly when it is obvious that smoking (or the failure to use poly-unsaturated fats) is neither a sufficient nor a necessary cause of lung cancer and the other diseases associated with smoking. Out of ten heavy smokers, only one will die of lung cancer; hence clearly smoking is not a sufficient cause; there must be many other factors which, possibly in conjunction with smoking, produce a final result of death from lung cancer. Similarly, smoking is not a necessary cause; at least 1 in 10 people who die of lung cancer is a non-smoker, and among the Mongoloid races the figure drops to about 1 in 2 (References given later, with detailed discussion). Likewise, many people who die of CHD (Coronary Heart Disease) are non-smokers. Thus there clearly is a highly complex net of causal factors, and a stress on any one of these is scientifically meaningless, particularly if their interaction is synergistic.

Early reports of a statistical association between cigarette smoking, on the one hand, and cancer and coronary heart disease, on the other led to extrapolations from these statistical data to possible savings of lives if people were to quit smoking, or never

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took it up.

According to reports of the U.S. Surgeon-General (1982), cancer was responsible for approximately 412,000 deaths in the United States; the report estimated that in 1982 there would be 430,000 deaths due to cancer: 233,000 among men and 197,000 among women. It claimed that 22%-38% of these deaths "can be attributed to smoking, and therefore are, potentially, avoidable" if smoking did not exist in human behaviour. The report clearly suggests a causal interpretation of the statistical association between smoking and lung and other cancers, and it is this interpretation of the data which has been criticized by many experts, such as Berkson (1958), Berkson and Elveback (1960), Boscombe (1965), Burch (1976, 1978, 1983, 1986), Eysenck (1986), Fisher (1959), Katz (1969), Mainland and Herrera (1956), Oeser (1979), Seltzer (1989), Sterling (1976, 1977), Yerushalmy (1966) and others. The purpose of this book is to examine the claims made by the supporters of this "orthodox" view in light of the criticisms made by leading statisticians, epidemiologists and oncologists, and to attempt to decide to what extent the claims made for this view are scientifically acceptable. In a later section, an attempt will also be made to consider facts and data not accommodated by the "orthodox" view, such as the relationship between personality and cancer and between stress and cancer. We will also examine some alternative theories. Lastly, we will consider similar data in relation to coronary heart disease, which is also often claimed to be statistically and causally related to smoking. The evidence here has been equally subject to criticism, and this will be reviewed in some detail. Here, too, there may be alternative theories which explain many of the facts not covered by the orthodox view.

The theory that smoking plays a causal role in the etiology of

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cancer, coronary heart disease and various other disorders has given rise to speculation, as already mentioned, about the number of lives that could be saved if smoking could be prevented. Burch (1978) quotes studies by Higginson and Doll, claiming that we should be able to reduce the incidence of cancer "by at least 80%-90%" if cigarette smoking could be eliminated, and the U.S. Surgeon-General's Report (1982) states that "it is estimated that 85% of lung cancer cases are due to cigeratte smoking," and that consequently "85% of lung cancer mortalities could have been avoided if individuals never took up smoking." In a speech on January 11, 1978, the Secretary of the Department of Health, Education and Welfare in the United States, Joseph Califano, stated that in 1977, smoking caused 220,000 deaths from heart disease, 78,000 from lung cancer, and 22,000 from other cancers, including bladder cancer, for a total of 320,000 deaths. One month later, Secretary Califano attributed to cigarette smoking 15,000 deaths from chronic bronchitis and emphysema, 125,000 from heart disease, and 100,000 from cancer, and stated the total to be "more than 320,000." No source was given for any of these figures, and no explanation given for why chronic bronchitis, and emphysema were included in the February total but not in the January one. He also failed to explain how his estimate of smoking accounts for 40% of all cancer deaths yearly, double that suggested by the American Cancer Society.

In a similar vein, Dr. David Owen, former Minister of Health and Social Services in the United Kingdom, stated that 50,000 deaths in the United Kingdom were due to smoking, and could have been prevented by people stopping smoking.

Similar sums have been done recently in Europe. Thus a recent report by Roos, Vernet and Abelin (1989) gives rather imaginary

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figures for the number of deaths caused by smoking in different Swiss cantons, basing its conclusions on the hypothesis that lung cancer is caused to an extent of 90% in males and 50% in females by cigarette smoking, and that bronchitis and emphysema are so caused in 75% and 60% of all cases, respectively. Atteslander (1989) has cogently criticized this report on grounds which also apply to many other similar publications - lack of care in handling official statistics, confusion of definitions and eccentric calculating methods; difficulties in establishing cause-effect relationship; and many others.

As many others have done before, Abelin (1984) and the World Health Organization (1988) draw the conclusion that what is needed is a campaign to eradicate smoking, assuming that, in the words of Vecchia, Levi and Gutzwiller (1987) smoking is "une epidemie evitable".

Of particular interest is "The Big Kill", a 15-volume document launched by The Health Education Council jointly with the British Medical Association, one volume being issued for each of the 15 regional health authorities in England and Wales. According to this publication, smoking annually kills 77,774 people (55,107 men and 22,667 women in England and Wales, from heart disease, lung cancer and bronchitis/emphysema. And because of their smoking, some 108,218 people are hospitalized each year with these diseases. As Burch (1986) comments: "The biologically ignorant but numerate reader will be forgiven for concluding that epidemiology is not only a rigorous science but an incredibly accurate one, with an implied error in mortality estimates of less than 1 part in 77,774." (p. 1956.)

The latest report of the U.S. Surgeon General (1989) continues this type of argumentation. He states that "smoking will continue as

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the leading cause of preventable, premature death for many years to come... As a result of decisions to quit smoking or not to start, an estimated 789,000 smoking-related deaths were avoided or postponed between 1964 and 1985. Furthermore, these decisions will result in the avoidance or postponement of an estimated 2.1 million smoking-related deaths between 1986 and the year 2000." (p.IV). Can this really be true?

Burch (1986) raises two questions. The first relates to the recording and certification of the cause of death. To show the utter unreliability of such figures, he quotes a study by Heasman and Lipworth (1966), who surveyed reports from 75 hospitals, comparing the clinicians' diagnoses of the cause of death with the pathologist's necropsy report. Taking as our example lung cancer, clinicians diagnosed 338 cases while pathologists discovered 417 cases post mortem. However, in only 227 instances was agreement obtained! If the pathologist's report were correct, then 111, or 33% of the clinicians' diagnoses were false-positive, while 190 genuine cases (46%) of lung cancer were missed. This is a terrifying error rate when we consider that all the published estimates of death from smoking are based on such worthless figures. The issue of unreliability of death certificates is so vital that we will return to it in some detail later.

Burch's second point is equally important. It relates to the question of how a <u>statistical</u> association between smoking and disease is converted into a <u>causal</u> estimate of the proportion of deaths due to smoking. As the Royal College of Physicians (1971) admits, "It is not possible to give a precise estimate of the proportion of these excessive deaths among smokers which are caused by smoking. There can be little doubt that at least half the estimated 31,000 excess deaths

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among male smokers, aged 35-64, in the United Kingdom, were due to smoking." As Burch comments: "This passage shows a recognition by the Royal College that not all of the association between smoking and mortality is necessarily causal. However, no procedure is described whereby an objective estimate of the magnitude of the causal contribution might be derived and the choice "at least half" would seem to be arbitrary." (p. 956.) Thus the unreliability of the estimates of cause of death is multiplied by the arbitrariness of causal attribution; why one-half rather than one-quarter?

The Royal College goes on making arbitrary attribution estimates. "It should not be unreasonable to attribute to cigarette-smoking 90% of the deaths from lung cancer, 75% from chronic bronchitis and 25% of those from coronary heart disease." For women, the Report acknowledges the greater difficulty of precise attribution, but goes on undaunted to say: "It can reasonably be assumed that at least 40% of the deaths from lung cancer, 60% of those from bronchitis, and 20% of those from coronary heart disease in women aged 35-64 may well be due to cigarette smoking." The sophisticated reader will be aware that expressions like "would not be unreasonable", "may well be due to" and "it can reasonably be assumed that", have no scientific standing or meaning; they refer simply to guesses which can easily be doubled, or halved. Thus "The Big Kill" raises the percentage of deaths from cigarette-smoking for lung cancer in women from 40% (Royal Society) to 80%, without batting an eyelid. Such estimates are meaningless, even if the figures for the statistical association between smoking and disease could be accepted. As we shall see, that is by no means so; these figures are based on studies characterized by a combination of poor methodology and faulty reasoning.

Burch summarized his conclusions from these considerations as

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follows: "We have to bear in mind that the reports of the Royal College of Physicians and of the U.S. Surgeon-General were prepared by committees with a predominantly medical background and outlook. Their primary concern, therefore, is likely to have been with the avoidance of unnecessary suffering and premature death. No one can quarrel with these aims and the good intentions permeating the reports. The process of reaching sound conclusions about causation is, however, more of a scientific than a medical task. Medical skills are required, of course, to reach an accurate diagnosis of the cause of death and a proper appreciation of limitations in the evidence, but analysis of the resulting statistics calls for familiarity and dexterity with scientific logic. The two skills are not incompatible but they are not always combined in the same person. We may note that Feinstein, (1979), himself both a distinguished clinical epidemiologist and an expert medical statistician, protests that a "licensed" epidemiologist "...can obtain and manipulate the data in diverse ways that are sanctioned not by the delineated standards of science, but by the traditional practice of epidemiologists."

What are these "traditional practices?" The U.S. Surgeon-General reproduces in his 1982 Report a passage from his first report about smoking and health published in 1964. It encapsulates a methodology-cum-philosophy that enjoys a wide support among epidemiologists: "...the causal significance of an association is a matter of judgment which goes beyond any statement of statistical probability. To judge or evaluate the causal significance of the association between an attribute or agent and the disease, or the effect upon health, a number of criteria must be utilized, no one of which is an all-sufficient basis for judgment. These criteria include: (a) the consistency of the association; (b) the strength of

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the association; (c) the specificity of the association; (d) the temporal relationship of the association, and (e) the coherence of the association." The inadequacy of these poorly defined criteria and the dubious manner of their application to the association between smoking and lung cancer have been discussed at length elsewhere (Burch, 1983). With reference to (c), Browntree (1965) commented: "the way it (the 1964 Report) claims the facts are in conformity with the criterion is to flatly ignore the facts". That comment remains applicable not only to (c), but to all five criteria. Subjective judgment, on which the U.S. Surgeon-General places repeated emphasis, should play as limited a role as possible in epidemiology as in other sciences. For how do we distinguish between judgment and prejudice? "Scientific analysis aims to replace subjective judgment by the objective testing of hypotheses." (p. 957.)

With these conclusions it is difficult to find fault, and the rest of this book is devoted to a consideration of the evidence, and the conclusions which may justifiably be drawn from this evidence.

There is one additional point to be considered in connection with the statements by the Royal College of Physicians and the Surgeon-General of the United States, concerning the number of deaths directly due to smoking. The statement quoted about the "excess deaths among smokers which are caused by smoking" are not really intelligible without being related to a precise model of causation.
What precisely does it mean to say that 40% (or 80%!) of deaths from lung cancer in women are due to cigarette smoking? There are several models which might serve to mediate such interaction between smoking and disease.

The first model asserts that out of 10 deaths from lung cancer in women, 4 (or 8) are directly and solely due to smoking. This simple-

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minded model can hardly be intended to be taken seriously, but the arguments advanced by the U.S. Surgeon General, and the Royal College of Physicians, often seem to assume its correctness. The notion that other risk factors than smoking play absolutely no part in these deaths conflicts with all we know about smoking and its many connections with other risk factors (drinking, stress, style of life, etc.), and is quite untenable.

A second model would assert that there are many risk factors for lung cancer (or coronary heart disease, or whatever disease is linked with smoking), and that in every sufferer from lung cancer 40% (or 80%) of these risk factors are constituted by cigarette smoking. This scenario too is unrealistic; it is simply not reasonable to assume that the proportion of all risk factors contributing to disease would be identical for all sufferers, and there is solid evidence to contradict it, as will be shown in later sections. This model, too, seems often to be assumed by writers on the subject.

A third model would assert that risk factors are unevenly spread among sufferers, so that the percentages mentioned only apply <u>on average</u>, but not in any particular case. Thus for a smoker who has been in touch with asbestos the percentage due to smoking might be only 10%, while for someone else not associated with any other risk factor the percentage might be 100%. This model seems more realistic, but of course it suffers from the fact that there is no known method of calculating the importance of risk factors for individuals. The model also makes the unlikely assumption that risk factors act in a simple <u>additive</u> fashion; as we shall see presently, the evidence strongly opposes such a view.

We come finally to the fourth model, which seems to be more in accord with the facts than any of the preceding ones. It asserts that

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smoking-linked diseases are caused by multiple risk factors combining in a synergistic fashion, i.e. the interaction is multiplicative rather than additive. The evidence for this model will be discussed in a later section, but we may here mention some of the papers supporting this view (Grossarth-Maticek, 1980, 1989; Grossarth-Maticek, Vetter, Frentzel-Beyme and Heller, 1988; Grossarth-Maticek, Eysenck & Vetter, 1988; Eysenck, 1988). The evidence suggests very strongly that smoking by itself has no effect on cancer or coronary heart disease; in samples free from other risk factors, smoking does not correlate at all with these diseases. It is only in combination with other risk factors (in particular psychosocial ones) that smoking shows statistical associations with these diseases. Whether these statistical associations can be interpreted in a causal manner is still an unsolved question.

Dembroski (1984) comes to conclusions similar to ours when he writes that "the findings reviewed clearly indicate that there are very complex relationships present involving classic risk factors, stress, personality attributes, consummatory behaviors, and physiologic reactivity. Moreover, the observation that many consumatory behaviors covary, e.g. cigarette smoking, caffeine, alcohol, etc., and that each can affect cardiovascular reactions to challenge, makes it clear that sorting out individual and interactive effects is a complex challenge for future research. Even more difficult will be identification of the Central Nervous System (CNS), the Autonomic Nervous System (ANS) and related mechanical and neuroendocrine processes operating during interactive effects as well as gaining a precise understanding of how such processes are related to pathophysiological mechanisms in atherogenesis and clinical CHD. At the very least, new findings in

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this arena offer more evidence of the importance of primary and secondary prevention programs. In designing such programs, one might well consider that the two separate categories of risk factors (physical and psychosocial) are not so separate after all." (p.19)

The postulation of a proper model for the interaction of risk factors is vital for the appreciation of such statistical calculations as those quoted from the U.S. Surgeon-General or the Royal College of Physicians. In the absence of such a model the figures are meaningless, even if cause of death had been reliably assessed (which it had not), and even if a proper method of calculating causal determination from statistical association had been established (which it had not). On all these grounds, then, we must conclude that the figures for deaths-from-smoking so often publicized have no scientific basis. It is unfortunate that official publications usually just repeat the kinds of calculations discussed above, and fail to answer legitimate criticisms, or to spell out the precise nature of the models of interaction assumed. It is difficult to understand this reluctance to accept the existence of problems and anomalies in the argument that smoking causes disease, or to deal constructively with objections. The issue is of fundamental importance socially, medically and scientifically, and should be so treated.

These inadmissible projections derived from faulty data have been taken up with enthusiasm by the Press, which, taking these estimates seriously, has sensationalized these improbable and unproven estimates to an extent which has convinced large numbers of lay people, and also medical people not intimately familiar with the evidence, that indeed smoking is responsible for a large majority of the deaths from cancer and coronary heart disease. Clark (1989) has demonstrated very clearly, by an analysis of the way the topic has been treated by

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quality papers, that objectivity was completely abandoned by the journalists involved, and that a bandwaggon effect was created which in turn promoted medical efforts to find more and better evidence for these doubtful propositions. As Clark points out, there was an almost complete absence of reports that there existed a controversy in this field, and a complete avoidance of balance concerning such issues as public smoking, passive smoking, and tobacco sponsorship in advertising.

This lack of objectivity is a serious matter in issues concerning general health questions, but it may have more serious implications as suggested in a paper by Grossarth-Maticek and Eysenck (1989) showing that media information that smoking causes illness is a self-fulfilling prophecy. It was found there that smokers who obtained their information concerning the possible deleterious effects of smoking on health from the media only, showed a significantly higher death rate than did smokers who derived this information from self-observation, or who did not believe it. Thus the extremly one-sided way in which the Press has treated this issue shows a lack of responsibility which may itself cause stress, and through stress increase the chances of people who derive their information from the Press to die of cancer and coronary heart disease.

In this introductory section we have not made any attempt to discuss evidence suggesting that writers supporting the orthodox view are not entirely along the wrong lines, or refute evidence concerning the claims that smoking causes deaths from cancer and coronary heart disease, or that passive smoking has similar effects (Saracci and Riboli (1989); this will be done in later sections. In this section the intention was merely to draw attention to the fact that there was an on-going debate concerning different models of interaction between

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risk factors and disease; that the existence of such a debate had been almost completely disregarded by the Press, and even by authoritative publications by the Royal College of Medicine in the United Kingdom, the Surgeon General in the U.S.A., and the World Health Organization. It was further suggested that the estimates of the number of lives that could be saved if only people were to quit smoking, or never took it up, had little scientific basis, and again we will document this in later sections.

In the next section we will take up the question of what empirical evidence there is about the effects of giving up smoking, and the extent to which this evidence supports the "orthodox" view. We will then examine in more detail the validity of the evidence concerning a statistical relationship between smoking and disease, and the acceptability of a causal inference concerning this relationship.

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(2) Does quitting smoking save lives?

Claims like those of the U.S. Surgeon-General (1982) that giving up smoking lowers lung cancer and other types of mortality is of course a vital one for any consideration of possible relations between smoking, cancer and coronary heart disease. There are two ways of studying such effects. The first one takes a sample of subjects, usually relatively homogeneous, (e.g. British physicians), follows them up and looks at the death rates from various causes of those who give up smoking, and those who continue to smoke (Doll and Peto, 1976). The alternative method is to form two groups, matched on as many relevant variables as possible, and to consider one of these as a control, receiving no instruction, while the other is a therapy group receiving instructions as to giving up smoking, and possibly also receiving advice relating to other risk factors, such as poor diet, high blood pressure, etc. Unfortunately practically all the positive results of giving up smoking have been reported from studies using the first of these methods, i.e. self-selection, and it is widely recognized that no relevant conclusions regarding causality can be drawn from studies of self-selected populations only. It is now quite clear that this is a crucial factor making it impossible to compare ex-smokers and continuing smokers with the aim of establishing the causal link between smoking and disease. Friedman et al. (1979) have shown that ex-smokers and continuing smokers are already very different from the point of view of health at the time that the ex-smokers give up smoking, and Eysenck (1980) has shown that with respect to personality, ex-smokers are more like non-smokers than they are like continuing smokers. Thus the necessary conditions for the

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paradigm is not fulfilled, namely that ex-smokers and continuing smokers should be similar or identical from the point of view of personality and health at the time that ex-smokers give up smoking. It follows that no interpretation along causal lines can be made of the differential nortality rate of ex-smokers and continuing smokers.

The Friedman et al. (1979) study is particularly important in demonstrating the lack of comparability between smokers who continue to smoke, and smokers who quit smoking. The study concerns white and black men and women who had had three or more examinations concerning their health. The authors compared ex-smokers and continuing smokers for a large number of characteristics associated with risk of coronary heart disease; assessments of these characteristics were made at a time when all were smoking cigarettes. Persons who remained non-smokers provided an additional comparison group. It was found that smokers who later quit showed statistically significant differences from smokers who continued smoking, in certain cardiovascular symptoms, social and personal charactistics, smoking intensity, and some other traits. Compared with persistent smokers, quitters in most or all race-sex subgroups had higher relative weight and lower alcohol consumption, but smoked fewer cigarettes for shorter duration, inhaled less, had higher vital capacity, lower leukocyte count, lower prevalence of abnormal electrocardiogram, less exertional chest pain, exertional dyspnoea, and exertional leg pain, higher educational level, and a tendency to answer a psychological questionnaire less like persons who later developed myocardial infarction. Other coronary heart disease-related characteristics such as cholesterol and blood pressure showed small differences. It is important to note that controlling for smoking quantity had little effect on differences between the persistent quitters and persistent smokers for certain

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characteristics which seemed likely to be smoking-related. For several characteristics, quitters were more similar at index examination to never smokers than to persistent smokers. Similar results were obtained in the famous Framingham study, although the numbers involved were too small to give incontrovertible evidence. In all instances, persistent smokers and quitters had directional differences similar to those found in the Friedman et al. study.

The results of this study should not be taken to mean that follow-up studies of self-selected quitters and smokers do not give important information. The study merely suggests that the situation is a very complex one, and that detailed medical and psychological examinations must be made of quitters and consistent smokers prior to the time when the former quit smoking. A complex statistical enquiry could then be undertaken to estimate the degree to which quitting had an effect independent of the already existing differences in disease-related characteristics. Methodologically all the existing studies are so flawed that no sensible conclusions can be derived from them. It is unfortunate that many publications draw conclusions from these studies without mentioning the contamination pointed out by Friedman et al, or the necessity of taking these considerations into account.

From a general point of view, the study of the Multiple Risk Factor Intervention Trial Research Group (1982) is an example of the type of study of groups which are not self-selected, but include a measure of randomization. In this randomized primary prevention trial to test the effect of a multifactor intervention programme on mortality from coronary heart disease, 12,866 high-risk men aged 35-57 years were randomly assigned either to a special intervention programme consisting of drug care treatment for hypertension,

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counselling for cigarette smoking, and dietary advice for lowering blood cholesterol levels, or to the usual resources of health care in the community. An average follow-up period of 7 years showed that risk factor levels declined in both groups, but to a significantly greater degree for the experimental group. Mortality from coronary heart disease was 17.9 deaths per thousand in the experimental group and 19.3 deaths per thousand in the control group, a statistically non-significant difference. Total mortality rates were 41.2 per thousand in the experimental group and 40.4 per thousand in the control group, that is, mortality was greater in the experimental than in the control group. Thus, the effect of lowering significantly the consumption of cigarettes (as well as significantly lowering blood cholesterol levels and also lowering bood pressure) was practically non-existent; the slightly greater mortality rate for the experimental group can hardly be taken seriously. The results as far as coronary heart disease are concerned will be discussed again later on; the overall mortality rate, however, is important because it includes cancers, and should have declined as a consequence of the lower levels of cigarette consumption in the experimental group. This is important in view of the statement, made in the U.S. Surgeon-General's Report (1982, p. 5), that "Cigarette smokers have overall mortality rates substantially greater than those of non-smokers," and that it would be expected that giving up cigarette smoking would reduce these overall mortality rates. Apparently this is not so overall, and, as other studies have shown, it is not so with respect to cancers specifically.

There have of course been attempts (e.g. Oliver, 1982) to explain away the disappointing results, and undoubtedly the 115 million dollar experiment was badly designed and poorly executed. (Jarvis et al., (1984) have criticized particularly the methods used to measure

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smoking activity). In particular, it lacked appropriate psychological expertise in looking at stress and personality factors which are known to influence the outcome (Eysenck, 1985). Nevertheless, the study does show that even on such a very large scale there is no evidence of any effects for cessation of smoking to increase chances of survival. The data have been analysed for small subgroups, with slightly more positive outcome, but such a procedure is statistically inadmissible when the overall result does not significantly bear out the theories under investigation, or even shows opposite outcome.

It should be noted that other trials, such as the continuing World Health Organization European Trial, which comprises 63,733 men aged 49-59 in 44 parent factories in Britain, Belgium, Italy, Poland, and Spain (World Health Organization European Collaborative Group, 1982) also make depressing reading in that changes were smaller than expected and not completely consistent or sustained. The authors found that, despite an estimated fall of 14% in coronary heart disease risk in the whole group and of 24% in the high-risk subgroup after 4 years, no equivalent fall in incidence of coronary heart disease might be shown even in a study of this size. Similarly, in the North Karelia project (Puska et al., 1979), an overall mean net reduction of 17% in men and of 12% in women occurred 5 years after inception with regard to cigarette smoking, blood pressure, and plasma cholesterol concentrations in the intervention community, compared with the control community, but here also there was no reduction in mortality from coronary heart disease. Only the small-scale Oslo study (Hjermann et al., 1981, Holme, 1982) succeeded in showing a reduction in the incidence of coronary heart disease with cessation of smoking and dietary intervention to lower lipid concentrations in non-hypertensive men in high-risk categories. This combination of smoking

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cessation and cholesterol reduction makes interpolation difficult. Overall, the outlook is not promising, although better-designed, better-controlled and longer- continued studies might alter the outlook. All one can say is that attempts to prove the influence of cigarette smoking as a causal factor in disease by means of trials avoiding the obvious error of self-selection have not on the whole been successful.(1)

Methodologically superior to any of these studies is a report by Rose and Hamilton (1978) in which a randomized controlled trial of smoking cessation is reported for 1445 male smokers aged 40-59 at high risk of cardiorespiratory disease. Marked differences in amount of smoking were observed in the intervention groups, as compared with the control group; 51% of the intervention group reported that they were not smoking any cigarettes and most of the others reported a reduction. Nevertheless, as the authors report, "Disappointingly, we find no evidence at all of any reduction in total mortality." (p.280). They did find some improvements in minor symptoms, such as coughing, and in chronic sputum production in men with early chronic bronchitis; many also reported a lessening of dyspnoea, but airways obstruction did not improve.

The studies so far mentioned have all dealt in the main with coronary heart disease, and it might be thought that the results might not apply to lung cancer. There is, however, the report by Rose et al. (1982) of a ten-year follow-up study of middle-aged male smokers at high risk of cardiorespiratory disease who were allocated randomly to an intervention or a normal care group. The intensive advice given to the first group was successful in reducing the average consumption of cigarettes by just over one half in this group. In the normal care group of 731 men, 25 cases of lung cancer were reported; in the

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Footnote, p.22.

(1) In addition to the trials mentioned, there have been several others, such as the Oslo study (Leren et al., 1975), and the Finnish Businessmen's study (Miettinen et al., 1986), in which smoking-reduced groups were compared with control groups. In the six major studies, none showed a significant difference in total mortality, in CHD mortality, or in cancer mortality. So much for the alleged beneficial effects on mortality of giving up smoking!

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intervention group of 714, there were 22 comparable cases - a non-significant difference. Data for all deaths in these groups are free from diagnostic error, and are hence the most reliable: 17.2% in the intervention group died compared with 17.5% in the normal care group, giving a negligible and statistically non-significant difference. Thus, this study gives results similar to the other intervention studies using randomized groups - a failure to detect any effect of giving up smoking. Curiously, Rose et al. found at a significant level of $p < 0.003$ that the intervention group subjects had a much higher rate of "all cancers other than lung cancer" than the non-intervention group subjects; whether this result can be replicated is, of course another matter, particularly since there are difficulties in assigning a valid probability value to an a posteriori hypothesis. Burch (1983) comments that, for all these studies, the results for total mortality are entirely in line with the analysis of temporal trends of sex- and age-specific mortality from all causes in the whole of England and Wales (Burch, 1983), which "failed to detect any causal influence of cigarette smoking when consumption was rising and no prophylactic influence when consumption was falling" (p.832).

We have not reviewed all the many studies looking at the effects of cessation of smoking on coronary heart disease, but such a summary has recently been published by McCormick and Skrabanek (1988), under the challenging title of "Coronary Heart Disease is not Preventable by Population Interventions". As they point out: "This review of the present experimental evidence that we can prevent much coronary heart disease provides no data to justify the time, energy, and money which are being devoted to this crusade.....to base population strategies on unproven hypotheses seems unreasonable." (p.841.) Several authors (e.g. Gunning-Shepers et al., 1989; Fries et al., 1989) have tried to

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point out certain redeeming features in the evidence, but they do not seriously deny the major conclusion in the McCormick & Skrabanek study.

It is interesting to note that well-meant suggestions based on ignorance or faulty research studies may in fact decrease rather than increase survival. Thus the recommendation that we should seriously lower our cholesterol level through diet changes or drugs, in order to reduce the incidence of CHD. Yet cholesterol plays a vital role within the body, and reductions in cholesterol level may have disastrous consequences. Oliver (1988) has recently reviewed the literature, and concludes that "reducing cholesterol does not reduce mortality" (p.814). He finds that the evidence shows an inverse relation between serum cholesterol and cancer, which might or might not be causal. He shows that "the frequent claims that thousands of lives will be saved by reducing plasma cholesterol are unsubstantiated", and explains that "most extrapolations from epidemiologic data and simulation models fail to take into account the differential effect that cholesterol reduction seems to have on each of the three main end points - non-fatal cardiac events, cardiac deaths and non-cardiovascular deaths, (p. 815). Finally, he warns against the evangelical publicity campaigns that are being waged in favour of cholesterol reduction; as he says, "the issue is a very serious one if vast sums are spent and widespread changes are made in the lifestyle of normal people when the accumulated evidence is that total mortality is unchanged or possibly even increased." (P. 815.) Mutatis mutandis much the same could be said about the anti-smoking campaigns!

One further point relating to non-smoking as a defence against disease may be mentioned, namely the suggestion that there is a

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correspondence of lung cancer mortality among different populations with different tobacco consumption rates (Lyon et al., 1980.) The point they made is that Mormons and Californian Seventh Day Adventists, i.e. non-smoking groups, have low incidence of lung cancer.

The membership of such groups, of course, involves self-selection, or descent from self-selected progenitors, but even overlooking this obvious point, the results present difficulties for the orthodox view, as Enstrom (1980) concluded after a careful examination of the evidence. According to the simple causal hypothesis, Mormons, who refrain from smoking in accordance with the dictates of their religion, should have an incidence of lung cancer the same as that which is found in comparable non-smokers of the general population. Lyon et al. (1980) compared the incidence in Mormons with that in non-Mormons (smokers and non-smokers) in Utah over the period 1967-75, finding an age-adjusted incidence of lung cancer in male Mormons of 46% of that in male non-Mormons; for females the incidence was 44%. Comparing the Mormons with non-smokers only, it would appear that, on the basis of the orthodox view, the incidence of lung cancer in male Mormons is at least twice that expected for a population of non-smokers who are not Mormons. "On the constitutional hypothesis, the Mormon population - involving selection - comprises a mixture of never-smoking and smoking genotypes with, among males at least, a relatively high proportion of the former" (Burch, 1983, p.832). The cancer mortality patterns in Mormons are "not clearly explained by their smoking habits" (Enstrom, 1980).

Actually, a suitable use of published data comparing Utah with matched other states of the U.S.A. can be used to test the hypothesis that a 50% lower rate of smoking and drinking would save large numbers

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of lives. The following calculations are quoted from an unpublished analysis by Dr. Miron Johnston (personal communication). He comments: "...that the low mortality rate in Utah (5.5 deaths per 1000 population, as compared with 8.7 for the total U.S.) is often cited as "proof" that abstention from alcohol, tobacco and caffeine puts the Mormons in Utah at considerably lower the average risk of premature death. (Per capita beer and cigarette consumption in Utah is consistently about half that of the total U.S.)"

Low crude mortality rates have to be corrected for age differences and racial composition. Using age specific mortality rates, and comparing Utah with the Plain States (North and South Dakota, Nebraska, Kansas, Minnesota and Iowa), which resemble Utah demographically in terms of climate, ethnic mix, and population density, we can obtain figures freed of their obvious contaminating factors. These figures still contain deaths due to alcohol abuse, i.e. deaths due to drunk driving, alcohol-caused liver disease, etc. This leaves us with just 4,173 premature white deaths attributable to a combination of caffeine, tobacco and alcohol used in moderation. (From this we should probably subtract at least some of the 9826 white deaths under age 75 attributed to "cirrhosis of the liver and other unspecified chronic liver diseases without mention of alcohol", a frequent omission on death certificates!) Such a difference, less than 4,173 deaths, considering the very large numbers involved, is minute, even if we disregard the final correction suggested; it gives no support to the suggestion of hundreds of thousands whose lives could be saved by abstinence from smoking! Thus a realistic comparison of populations differing in smoking and drinking habits by some 50% suggests a negligible difference in mortality.

Just as the alleged effects of smoking have ended in disarray, so

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have the alleged effects of diet on CHD. Already in the late-Seventies, Mann (1977) and McMichael (1979) announced "an end of an era", and held an inquest "on the topic". As the latter points out, "all well-controlled trials of cholesterol reducing diets and drugs have failed to reduce coronary (CHD) mortality and morbidity. (p.173.) Recognition is now dawning that a low fat content diet, concentrated on polyunsaturated fats, may even be harmful in inducing cancer, although the evidence for this does not at present seem strong enough to formulate any conclusions (Schatzkin et al., 1988). Let us merely note, as Le Fanu (1987) has pointed out, that medical advice based on so-called epidemiological evidence, follows fads which are often contradictory, and not based on proper scientific evidence, and finally fail, in order to be succeeded by other fads. The possibility cannot be ruled out that the anti-smoking campaign may be such another fad; certainly there is no evidence in the studies reviewed that quitting smoking has any strong beneficial effects on survival, or on the avoidance of cancer and coronary heart disease. As Burch (1986) has put the question: "Can epidemiology become a rigorous science?" On the basis of the existing evidence, one would hesitate to give a positive answer to the question.

One further study deserves special mention here because of the rather paradoxical results, and also because of the well deserved fame this study has received as a function of its methodological excellence. The study is the Framingham Heart Study. In 1974, Gordon et al. (1974) reported data for a twelve-year follow-up study. For male cigarette smokers, aged 45-74 at entry, who subsequently stopped smoking, the attack rate for coronary heart disease (other than angina-pectoris) was found to be "half that experienced by those who continued to smoke". This finding has become the most widely

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quoted evidence for the belief that stopping smoking dramatically reduces the risk of coronary heart disease.

As Seltzer (1989) has pointed out, however, this evidence is seriously compromised by an important omission. In the comparison of risk for continuing and quitting smokers, no data were cited for the analogous heart attack rate of never-smokers. Seltzer obtained evidence on this point for various follow-up periods, and the results are shown in Table 1. It can be seen that the coronary heart disease rate was higher for never smokers than for ex-smokers; at a twelve year follow-up point, the age-adjusted incidence of coronary heart disease was 8.3/100 for ex-smokers and 12.0/100 for never-smokers. Four additional analyses at various follow-up points are given in Table 1, showing that the coronary heart disease rates for never-smokers are from 23 to 67% proportionately higher than for ex-smokers. These results are truly extraordinary, and completely contradict the view that smoking causes coronary heart disease, and that giving up smoking will improve one's chances of survival. Such a hypothesis requires a linear relationship between never-smoking, quitting, and continuing to smoke; the existence of a very strong curvilinear relationship makes any such interpretation impossible.

Table 1 here.

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(3) How strong is the association between smoking and disease?

So far we have taken for granted the existence of a strong statistical relationship between cigarette smoking and disease, particularly cancer and coronary heart disease. Such a relationship can be demonstrated along two rather different lines. The first of these is the cross-sectional method. Here we take a group of patients suffering from a given disease, and compare them with some form of control group which may be suffering from a different type of disease, or no disease at all, with respect to smoking habits. This method is obviously weak methodologically. Our choice of a control group is clearly crucial, but any particular choice may be faulted for a variety of reasons. The method depends a good deal on memory (When did you take up smoking? How many cigarettes did you smoke? What types of cigarettes did you smoke?), and memory is known to be faulty, and subject to falsification. There are many other weaknesses which we will discuss later on, but few epidemiologists would doubt that the second method to be discussed, namely that of the prospective study, is superior because it is not subject to these weaknesses.

In a prospective study a sample is chosen at a point in time (a), and followed up over varying periods of time; at time (b) we enquire into the health status of the probands, and ascertain death and cause of death, or incidence, as the case might be. This method too has weaknesses (probands may be lost through emigration, or there may be refusals to allow doctors to discuss incidence, etc.), but these can usually be controlled statistically or avoided in one way or another.

The most important follow-up study to have been undertaken is

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undoubtedly the Framingham Heart Study, which has been called the "cornerstone" of coronary heart disease epidemiology (Leaventon et al., 1987). This study covers more than three decades of surveillance of the substantial cohort of men and women, and has produced a mountain of data and several hundred publications. The leading Framingham Study investigators have interpreted the follow-up data on the relationship between smoking and coronary heart disease in a very positive manner, declaring that cigarette smoking is a "powerful contributor" to the aetiology of CHD (Dawber, 1980; Kannel, 1981). This refrain has been taken up by almost all commentators, and the Framingham Study is universally regarded as the strongest proof of the existence of an important and significant relationship between smoking and coronary heart disease.

The study cohort was obtained from a random subsample of the adult residents of Framingham, Massachusetts; the response rate was 69%. There was in addition a group of volunteers, whose differences from the originally sampled group were not considered to be important (Dawber, 1980). The final cohort consisted of 2282 men and 2845 women who were aged 29 through 62 years, and free from coronary heart disease at the initial examination. Members of the study received a standardized cardiovascular examination at entry, including information on habits, physical characteristics, and blood chemistry. Data so acquired included information on tobacco smoking, alcohol consumption, systolic and diastolic blood pressure, hematocrit, hemoglobin, serum cholesterol, phospholipids, uric acid, relative weight, vital capacity, electrocardiogram, and urinalysis for sugar and albumin.

After the initiation, participants were checked for cardiovascular disease every two years, in an investigation that

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included medical history, physical examination, blood and other laboratory tests, with coronary heart disease incident episodes being classified as myocardial infarction, angina pectoris, coronary insufficiency, sudden death, or coronary heart disease deaths. The follow-up period now extends over 30 years, and a large number of data are available to answer the question of the relationship between cigarette smoking and coronary heart disease. Such an examination of the existing data has been carried out by Seltzer (1989).

Table 2 shows the major results of his investigation. The important columns are those showing risk ratios, i.e. the ratio of cigarette smokers to non-smokers in the incidence of coronary heart disease. The ratio of 1.0 would indicate no relationship whatsoever between smoking and coronary heart disease; a risk ratio below 1.0 would indicate that smoking actually benefitted probands, whereas risk ratios above 1.0 would indicate that smoking was somehow linked with coronary heart disease. The risk ratio of 2 has been designated by Hutchinson (1968) and Wynder (1987) as the boundary of a weak association.

Table 2 here

What does the table show? For women, it shows that either there is no relationship at all between smoking and coronary heart disease, or an inverse one; several of the risk ratio variables are below 1.0. It is difficult to take these values seriously, but it is quite clear that there is no evidence at all here for any relationship between smoking and coronary heart disease. For the men the values are slightly above 1.0, although for the 30 year follow-up, using the total set of age groups from 35-84, the ratio is exactly 1.0,

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suggesting that if there is any relationship, it is very weak indeed, falling well below the 2.0 level. Thus the best and most frequently cited evidence for the notion that cigarette smoking is a "powerful contributor" to the aetiology of coronary heart disease completely fails to live up to this description; it shows that at best there is a very weak relationship for men, and none whatsoever for women.

Would the relationship be stronger for heavy smokers? It is possible that the relationship there might have been obscured by large numbers of light smokers, but this does not seem to be so. Smokers of 40+ cigarettes per day were found to have a coronary heart disease risk ratio of only 1.3 (Kannel and Gordon, 1970).

When associations are weak, it is an elementary rule that we should look for possible confounding factors. A search for such confounding factors would have to take into account the fact that Hopkins and Williams (1981) listed 246 suggested coronary risk factors in their survey! Only a few of these of course are available on the Framingham protocols. Seltzer (1989) carried out a multivariable analysis including, as previous ones had not done, data about Type A personality, which is believed to be coronary heart disease-prone, and when such psychosocial factors were included along with systolic blood pressure and serum cholesterol, cigarette smoking was not found to be a significant predictor of coronary heart disease or myocardial infarction in men, nor of coronary heart disease or angina pectoris in women. (Psychosocial factors, and Type A personality, will be discussed in a later chapter. The Framingham investigators also found that cigarette smoking does not make an independent contribution to cardiovascular disease when Fibrinogen is considered along with standard Framingham risk factors. (Kennel et al., 1987). Seltzer (1989) makes an interesting comparison of the conclusions of the U.S.

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Surgeon-General's reports on "cardiovascular disease" (1983) and the conclusions to be drawn from the Framingham Study. The major conclusion of the 1983 report is that "cigarette smoking is a major cause of coronary heart disease in the U.S. for both men and women." This conclusion is supported by statements that:

(1) In men, the incidence of coronary heart disease is two-fold greater in cigarette smokers than in non-smokers, and four-fold greater in heavy smokers;

(2) In women, the rates of coronary heart disease are lower than in men, but are commensurately higher when the smoking patterns are similar to those in men;

(3) The risk of developing coronary heart disease increases with the duration (in years) of cigarette smoking; and

(4) The cessation of smoking leads to coronary heart disease death rates that are substantially lower in the stopped smokers than are in the continuing smokers, and after ten years of nonsmoking, the coronary heart disease of former light smokers approximates those of non-smokers.

Seltzer (1989) gives a table (Table 3) which makes interesting reading. As Seltzer points out: "The Surgeon-General's views and other features of the "conventional wisdom" about cigarette smoking and coronary heart disease obviously depend on many other studies beyond those of the Framingham cohort, and on many other data that have not been cited here for the smoking/coronary heart disease relationship. The main purpose of this paper is simply to point out that for the critical relationships noted here, the Framingham data substantially disagree with the "conventional wisdom" and that the anomaly remains unexplained. Because of the unusual care and

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thoroughness with which the Framingham cohort was selected, followed, and examined, it is difficult to attribute the anomaly to some intrinsic error in Framingham's epidemiologic methods. The explanation for the discrepancy is an intriguing challenge for future research."

Table 3 here.

The finding in the Framingham Study that there is a very weak association, if any, between smoking and coronary heart disease makes it desirable to look at the possible strengths of a relationship between smoking and smoking-associated diseases, in the form of a meta-analysis, i.e. averaging across all available materials. Wakefield (1988) collected and reviewed empirical studies from the 1985 Smoking and Health Abstracts. The quality of the methods employed in each study was rated by two Ph.D. experimental psychologists who did not know the authors or results of the studies they rated. The relationships between smoking and the health variable (S) in each study were converted to a standard effect size and correlated for comparison. Results were presented for ten categories of health variables. The relationship between smoking and health were small for all categories with an overall relationship equivalent to a correlation of 0.13. Poorer studies yielded larger relationships between smoking and health than did methodologically stronger studies. A similar analysis of the 1982 Surgeon General's report produced an overall correlation of 0.17 between smoking and cancer. The relationship between smoking and disease as shown in recent empirical investigations is very weak and would be even weaker if only methodologically adequate studies were considered.

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As Wakefield points out, a major problem with the literature is its consistent reliance on the concept of the relative risk of a disease for smokers and non-smokers. Relative risk is conceptually the quotient of the probability of a disease for smokers and the probability of the disease for non-smokers, and is interpreted as the number of times the risk for non-smokers is increased for smokers (Fleiss, 1981). Usually computed by the "odds ratio", relative risk is a concept that is primarily useful for educational purposes rather than as a measure of the degree of association between two variables (i.e. smoking and disease). Relative risk allows an understandable way of communicating the "odds" involved in relationships between variables to persons with little or no statistical background; however, for conditions with small probabilities of occurrence, as is the case with most diseases, relative risk may be large, and consequently frightening, numbers resulting from trivial relationships. For example, five times a very small probability of developing a disease is still a very small probability of developing the disease. A better way of measuring the degree of relationship between two variables is with a correlation coefficient that expresses "no relationship" as a 0, and a "perfect relationship" as a 1. "The near zero effects for smoking and health variables estimated from all available literature abstracted in 1985 suggest an explanation of health problems in terms of simple causation by smoking is no longer plausible. Other alternatives, including personality, stress, genetic factors, and general lifestyle as leading to health problems....must now be considered more plausible than smoking." (p.473.)

It would be impossible in the limited space allowed to discuss all the many studies which have been done in this field, and the effort would not be worth the while because of the many methodological

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and statistical faults and errors so characteristic of practically all of these studies. More detailed discussions are available in Eysenck (1980, 1986). We will instead turn to a more general discussion of the available methodologies, and the type of error which is so characteristic of much of the work undertaken in trying to discover the relationship between smoking and disease. Let us just note, before passing on to these topics, that overall correlations of a size between .13 and .17, as discovered in the Wakefield analysis, are much too weak to be taken seriously, particularly as univariate studies of this kind cannot in the nature of things take into account other factors which may influence both the variables correlated. As Seltzer has shown in connection with the Framingham Study, when even a small number of other variables are taken into account, the apparent correlation between smoking and disease vanishes completely. The obvious fact that there are many risk factors in cancer and coronary heart disease makes univariate analysis pointless, yet the vast majority of studies have failed to employ the required multivariate paradigm.

One of the reasons why a multivariate paradigm is so necessary is concerned with the nomological network of intercorrelated factors which appears in every large-scale investigation of risk factors associated with smoking. Thus smoking is connected with personality, as we shall see in a later chapter, and it is also correlated with drinking, anti-social behaviour; low IQ; sexual behaviour, and many other variables (Eysenck, 1980). Figure 1, to take but one example, shows cumulative intercourse experience in college educated white males and females; it will be obvious that there are very large differences between regular smokers, quitters and never smokers at age 20; for instance, 63% of women who were regular smokers had had

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intercourse but only 23% of women who had never smoked! Thus if a correlation is found between smoking and cancer of the cervix, say, this association might be due entirely to the fact that more promiscuous women are more likely to develop cancer of the cervix (Eysenck, 1980). To discover whether smoking had a separate effect, we would have to ascertain, and partial out statistically, the effects of a promiscuous lifestyle. Given the large number of possible risk factors, such an exercise would be difficult, and certainly the vast majority of reports do not even make an attempt to rule out alternative hypotheses.

Fig. 1 here.

Perhaps more important than sexual precocity are eating and drinking. The average smoker household, for instance, spends 2 to 3 times as much as the non-smoker household on beer, and 73% more on coffee. Equally, smoker households relative to non-smoker households, spend a larger share of their food dollars on products we are told are bad for us (red meat and eggs) and less on foods that are supposed to be good for us (cereals, fruits, and vegetables.) This opens up the possibility that differences allegedly due to smoking (and passive smoking) may really be due to different drinking and eating patterns of different households. Certainly no statistics which do not control for this (and many other) smoking-correlated factors can be taken very seriously.

An alternative method to multivariate analyses of this kind, which may be difficult of even impossible in view of the large number of correlated risk factors, is the intervention study, in which one variable is experimentally manipulated, e.g. smoking, and the

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effects are noted. It is because of the inherent methodological superiority of this method that we have discussed the effects of quitting smoking in Section 2; the results, as we have seen, do not give any support to the view that smoking exerts a strong influence on the development of cancer and coronary heart disease.

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(4) The methodology of epidemiological studies of smoking.

What are the major arguments in favour of a close connection between smoking and disease, possibly interpretable in causal terms? The first argument, already considered to some extent, deals with the mortality ratios for different diseases, i.e. figures purporting to demonstrate that smokers of a given age and sex die more frequently of of a given disease than nonsmokers. The difference can be expressed as the "mortality ratio" (age-standardized mortality rate, or SMR) indicating the proportion of smokers to nonsmokers who are certified as having died of a particular disease. These ratios are usually in excess of 1.0 for a great variety of diseases, with the highest mortality ratio being that of cancer of the lung, followed by bronchitis and emphysema, and cancer of the larynx and the oral cavity. However, there are also mortality ratios below 1, e.g. for cancer of the rectum, 0.90 (Kahn, 1966), colorectal cancer in women (0.78 and 0.66 for women who smoked heavily - Hammond, 1966) and Parkinson's Disease (0.26 - Kahn, 1966; 0.81 for an older group - Hammond, 1966). Eysenck (1987) gives a survey of the literature; he stresses that these figures should not be taken to indicate a beneficial effect of smoking, just as the positive mortality ratios for lung cancer etc. do not necessarily indicate the nefarious effect of smoking; the problem of inferring causation from correlation is of course too complex for such easy inferences.

The second argument often advanced is that when mortality ratios such as those discussed above refer to the position of a particular country at a particular time, there appears to be a relationship between the crude male death rate for lung cancer and per capita consumption of cigarettes 20 years earlier, calculated over a number

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of countries; the time differences of 20 years is used because it is believed that smoking affects health only after lengthy periods of use.

A third argument is related to the fact that when mortality rates are examined by birth cohorts, it can be seen that most male and female cohorts, with increasing smoking prevalence, also have increasing age-specific mortality rates. In other words, there appears to be a correlation between the amount of smoking and prevalence of lung cancer over time (dose-effect paradigm.)

The fourth argument, already examined, relates to the alleged fact that quitting smoking will result in a lower mortality ratio, depending on the number of years since quitting smoking. These four arguments have been repeated time and again, and figures also given apparently to support them. We have already examined the figures on cessation of smoking, and found that these in fact do not bear out the "orthodox" view, but rather indicate that quitting smoking, when the proper controls are imposed on the study, has little or no effect on future coronary heart disease or cancer. We will now turn to a consideration of the other points raised, and the methodological and statistical weaknesses which make the argument invalid.

Before doing so, however, it is necessary to mention one point which is often alleged to prove a direct causal relationship between smoking and oral carcinogenesis. Much effort has been spent in finding animal models which might be used to support this view, and it is often claimed that studies have succeeded in finding direct evidence. This, however, is not true. As the U.S. Surgeon General's report (1982, p.89) makes clear, "The useful animal model for the experimental study of all carcinogenesis has not been found. Cigarette smoke and cigarette smoke condensates generally fail to

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produce malignancy when applied to the oral cavities of mice, rabbits or hamsters. Mechanical factors such as secretion of saliva, interfere with the retention of carcinogenic agents." Thus the statistical and epidemiological studies must bear the whole burden of the exercise; it is impermissible to quote animal experiments in this connection.

Turning now to the epidemiological data, we may perhaps begin by stating the obvious, namely that any conclusions that can be drawn from a statistical study of epidemiological data are dependent not only on the logic of the experimental design or the quality of the statistical analysis, but even more crucially on the quality of the actual data collected. If the data themselves are highly unreliable, and in particular when they are biased, erroneous conclusions may be drawn even though methodology and statistical analysis appear impeccable. The data epidemiologists mostly rely on are usually diagnoses made by a physician and recorded on the death certificate; data of this kind have been used in all the official reports by the U.S. Surgeon-General and the Royal College of Physicians, without seriously dealing with the question of misdiagnosis and reliability of data. Neither have these reports discussed the possibility of bias, which appears to be a very real danger in this field.

There has been a good deal of criticism of the use of statistics derived from diagnoses on death certificates; they have been generally considered as inaccurate and unreliable (Abramson et al., 1971; Beadeńkopf et al., 1963, Briggs, 1975; Wells, 1923; Willis, 1967). Surveys by Britton (1974), Cameron et al. (1977), Gruver and Freis (1957), Hartveit (1979). Heasman and Lipworth (1966), and Waldron and Vickerstaff (1977) have given ample support to these criticisms. Britton (1974), for instance, found that the reported frequency of

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disagreements between clinical and autopsy diagnoses ranges from 6% to 65%! If we regard autopsies as completely reliable criteria (an assumption which, as we shall see, is not entirely true), then clearly the amount of inaccuracy in diagnoses is unacceptable for serious statistical work.

Some quotations may give a rough idea of the consensus in this area. Bauer and Robbins (1972, p. 1474) state that "our study indicates that accurate clinical diagnoses of cancer are as much a problem today as they were a half-century ago." Abramson, Sacks, and Caban (1971, p. 430) state that "the death certificate data had marked limitations as an indication of the presence of myocardial infarction, cerebrovascular disease, pulmonary embolisms or infarctions....They gave a fairly accurate indication of the presence of malignant neoplasms but not of the specific sites or categories of neoplasms." And Britton (1974, p.208) concluded that "autopsies earlier did and still do reveal a considerable number of errors in clinical diagnoses....There is no convincing sign that the rate of errors had diminished over the years." So much for the accuracy of the data on which the "orthodox" view is based.

As an example of the most carefully planned and conducted work in this field, let us consider the study by Cameron and McGoogan (1981). They reported a prospective study of 1,152 hospital autopsies, comparing these with death certification in each case. They were merely concerned with the major disease leading to death as indicated by the physician filling in the death certificate. They found that the main clinical diagnosis was confirmed in 703 out of the 1,152 cases, or in 61%, leaving an error of 39%. This figure is not far removed from that observed by Britton (1974) in Sweden, where he found, in a careful, clinically controlled assessment, that main

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clinical diagnoses were confirmed in 57% of cases, leaving an error of 43%. Heasman and Lipworth (1966) and Waldron and Vickerstaff (1977) reported confirmed diagnoses in only 45% and 47.5% respectively, leaving error rates of 55% and 52.5%. It is small surprise that Cameron and McGoogan (1981, p.281) come to the conclusion that: "In our experience, statistics from death certificates are so inaccurate that they are not suitable for use in research or planning." If this be true, then clearly all the statistical work supporting the received view is based on extremely uncertain foundations.

One other item of interest emerged from the Cameron and McGoogan study: a marked increase in the proportion of diagnostic discrepancies with increasing age of the subjects. Below the age of 45 years, diagnoses were correct in 78%, but thereafter they fell off in a step-like manner with each succeeding decade until, over 75 years, fewer than half were confirmed. This has particular relevance to the incidence of lung cancer, as this of course occurs mainly in older men and women.

It is of interest to look specifically at data for neoplasms and for coronary heart disease diagnoses, as errors in these are of special relevance to the topic of this book. Cancer of the bronchus/lung was correctly diagnosed in 88 cases and wrongly diagnosed in 61 cases; thus the error rate is about the same as for all diseases. Bauer and Robbins (1972) looked at autopsies on 2,734 cancer patients, and found that 26% had clinically undiagnosed cancer; in a further 14% the condition was incompletely diagnosed, that is, cancer was suspected but its primary site was not known or was wrongly identified. Cameron and McGoogan conclude their comments on neoplasms by stating, "Carcinoma of bronchus was the most common neoplasm in our series and provided the largest group of misdiagnoses" (p. 294).

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Turning now to cardiorespiratory conditions, we find for acute myocardial infarct an agreement in 198 cases, and a disagreement on 109 cases - again an unacceptable level of error of diagnoses. Cerebrovascular disease scored an agreement in 129 cases and disagreement in 118 case, with an error rate of almost 50%. "The most common problem of differential diagnosis appeared to be in distinguishing it from cardiovascular disease," Cameron and McGoogan stated (p. 293). Hardveit (1979), Heasman and Lipworth (1967), and Klagan et al. (1966) also found a large amount of overdiagnosis and underdiagnosis of cerebrovascular disease.

Where diagnoses are as unreliable as they have been found to be in the case of lung cancer and coronary heart disease, we must be particularly concerned about the phenomenon of "detection bias," that is, the tendency of the physician to diagnose "smoking-related diseases" in smokers rather than in nonsmokers. Feinstein and Wells (1974) have published data to show that such detection bias is a reality, and might easily lead to false conclusions in the absence of careful necropsy examinations of the causes of death. Detection bias undoubtedly contributes part of the high mortality ratios for lung cancer often reported, and should be carefully excluded in any study purporting to have scientific validity.

Feinstein and Wells (1974) looked at 654 patients who were diagnosed after necropsy as having died of lung cancer. In this series, they studied the relationship between the rate of nondiagnosis during life and the amount of antecedent cigarette smoking. In patients whose history of cigarette smoking was unknown, this nondiagnosis rate wa 37%. The rate of nondiagnosis then portrays a distinctive downward gradient, falling from 38% undetected among non-cigarette smokers, to 20% among the light smokers, 14% in the

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moderate, and 10% and 11% respectively in the heavy and extreme smokers. "The data therefore suggested that the more patients smoke, the more likely they were to have the lung cancer detected during life," stated Feinstein and Wells (1974, p. 185).

Feinstein and Wells also investigated how this premortem detection gradient was related to the intensity of diagnostic examinations received during life by patients in their entire series, which included 677 cases which were diagnosed during life but received no necropsy. They used for this purpose the Papanicolaou cytologic examination (or pap smear) of the sputum. Since this test had not been obtained by all of their patients, its solicitation might have been affected by diverse factors, including the patient's smoking history. They therefore examined the pap smear research rate, and the results are in agreement with this hypothesis. The test was requested more frequently in smokers than in nonsmokers. Statistical tests showed that the trend was very highly significant. Detection bias was consequently found to be distinctly related to the amount of cigarette smoking.

There is no space to go into the other analyses done by Feinstein and Wells, which tend to support the general conclusion that "cigarette smoking may contribute more to the diagnosis of lung cancer than it does to producing the disease itself" (p. 184), and they go on to say: "It seems important to recall that in epidemiologic surveys of causes of disease, the investigators get data about the occurrence of diagnoses not the occurrence of diseases, and that the rates of diagnosis may be affected by bias in the way that doctors order and deploy the available diagnostic technology" (p. 184). Taken together with the general unreliability of diagnoses of lung cancer, these findings make it doubly improbable that the observed diagnostic data

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which furnish the foundations for epidemiological studies can be taken seriously by scientific investigators. More research is urgently required on the actual unreliability of diagnoses, as well as on "detection bias"; if reliable data on these two points were available, then possibly statistical corrections might be made to the published data on the relationship between smoking and lung cancer. Without such data, all conclusions are clearly based on very unfirm foundations indeed.

What light do these considerations throw on the problem of the apparent rapid rise in lung cancer over the years? This is copiously illustrated in the report of the U.S. Surgeon-General, together with the rise, 20 years previously, of cigarette consumption; it will be remembered that this temporal correlation is one of the major arguments put forward by epidemiologists in favour of the "orthodox" view. At the same time this apparent rise presents great difficulties for those who, like Burch (1976), Deser (1979) and Eysenck (1986), argue in favour of theories of the conception and development of carcinomas which are based on genetic hypotheses and largely disregard the role of external carcinogens. It is quite implausible to argue that there have been genetic changes of such a size and nature as to cause such manifold increases in the occurrence of lung cancer, and consequently the argument for the causal effects of environmental changes, air pollution and cigarette smoking, for example, must be taken seriously. An alternative suggestion is that the increase in deaths diagnosed as lung cancer has been due to improvements in diagnostic techniques, and is therefore more apparent than real. This argument has been put forward by Rigdon and Kirchoff (1953), who concluded that claims of genuine increase in the frequency of lung cancer were "open to question." Willis (1967, p. 187), after an

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extensive review of the literature, concluded: "It is not possible either to affirm or to deny that there has been a real increase." Similarly, Feinstein (1974) concluded his historical discussion by stating that diagnostic changes have played the most important role in the increase in death rate from lung cancer. Burch (1976) cites much evidence to support this view.

It seems certain that in the first years of the century lung cancer was considerably underdiagnosed. Sehrt (1904) described 178 cases of lung cancer discovered at necropsy, only six of which had been recognized during life. If we take this ratio of 172 failures to diagnose lung cancer as compared with six successful diagnoses of lung cancer, and argue that with our modern techniques all or most of the 178 cases of lung cancer would have been so diagnosed, then it seems quite reasonable to assume that much if not all of the apparent increase in deaths from lung cancer may have been due to improvements in diagnostic techniques.

The evidence suggests that at present there is a considerable overdiagnosis of lung cancer, and the question arises: What causes false-positive diagnoses? Rosenblatt (1969) has suggested that in the post-1930 period, false-positive clinical diagnoses of lung cancer have often been reported due to metastases in the lung from primary locations at many different sites. He too believed that the very great increase in recorded lung cancer deaths over the past 30 years was not due to an extrinsic carcinogen but resulted from the use of new diagnostic techniques, in particular, radiology, bronchoscopy, sputum examination, and surgery. He further suggested that the great interest in lung cancer stimulated by the theory that it might be due to smoking had produced a tendency to overdiagnose this particular disorder, and Smithers (1953) discovered that even specialists in

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thoracic diseases were guilty of a large proportion of false-positive diagnoses from 1944 to 1950.

Rosenblatt et al. (1971a,b) supported this argument by showing that at the doctors' hospital in New York, clinical diagnosis of lung cancer was over twice as frequent as diagnosis following necropsy. Carcinoma of the lung was the only neoplasm to be greatly overdiagnosed clinically, and in which no unsuspected cases were found at necropsy. Primary lung cancer had been simulated by pulmonary metastases from carcinoma of the pancreas, kidney, stomach, breast and thyroid, and by malignant melanoma. Burch (1976) makes the interesting comment: "It is of great interest that the 5.5% of lung cancers found in this recent New York necropsy series of malignancy is lower than a proportion found amongst several necropsy series from Austria, Germany and the U.S. published at the end of the 19th and beginning of the 20th century. In five subseries in which necropsy findings were the main basis of diagnosis, lung cancer diagnosis ranged from 8.3% to 11.5% of all cancers." This finding must throw doubt on the alleged increase in lung cancer.

The problem of metastasis to the lung being erroneously diagnosed as lung cancer is emphasized by a study reported by Burch (1978). He found that a total of 747 primary lung cancers was recorded in a large-scale post-mortem study of the anatomical distribution of metastases in Swedish cancer cases, but some 2,079 metastases to the lung from primary sites outside the lung! Burch gives many further instances, and it is difficult not to agree with him when he concludes: "There can be no doubt...that diagnostic artefacts have contributed massively to the secular increases in recorded death rates from lung cancer.... The beginning of the century was characterized by a severe under-diagnosis, especially above the age of 40 years" (p.

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458).

We have assumed in this section that autopsies will normally constitute a completely reliable criterion. However, it is fairly optimistic to imagine that diagnoses, even when based on autopsies, can be relied upon to give a true picture of the actual condition of the patient which caused death. In a recent editorial (1971) in the Annals of Thoracic Surgery, it was pointed out that: "The most experienced pathologists often disagree on classification of these tumours, and differential criteria are poorly defined." Large bodies of data are available to indicate that the reliability of medical diagnosis using pathological material relevant to respiratory diseases is well below what would be regarded as acceptable in psychological tests (see Kern et al., 1968; McCarthy and Widmer, 1974; Reid and Rose, 1964; Stebbings, 1971; Thurlbeck et al., 1968; WIlson and Burke, 1957; Yesner, 1973; and Yesner et al., 1965, 1973).

Autopsies, while greatly superior to death-bed diagnoses, are obviously still unreliable in that different experts have different views. Such unreliability makes validity suspect, although it would be difficult to give a numerical assessment of the degree of unreliability or the lack of validity in these data.

The difficulties introduced by errors in the certification of the cause of death make it desirable to study trends in overall mortality, rather than mortality due to specific diseases. Doll and Peto (1976) conducted a large-scale study of this kind and concluded that "much of the excess mortality in cigarette smokers could be attributed with certainty to the habit." Burch (1978) examined this conclusion and carried out a large-scale statistical analysis of smoking and mortality in England and Wales from 1950 to 1976, calculating percentage changes in sex- and age-specific death rates for all causes

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of death in England and Wales, by three-year periods. These changes in death rates were compared with corresponding trends and sex- and age-specific "constant tar" and "current" cigarette consumption in the United Kingdom. He concluded that: "No obvious cause-and-effect relation can be discerned" (p. 87). As he points out, the main problem is to explain the fairly consistent decrease in death rates in both sexes and all age groups during periods when cigarette consumption was either rising or falling. "The trends failed to support the hypothesis that smoking influenced mortality," he states (p. 87). Altogether he concluded that "This paper has shown that secular trends in overall mortality in England and Wales give no consistent indication that they were appreciably influenced by changes in cigarette consumption...on scientific grounds there can be little doubt that the conclusions drawn by the Royal College of Physicians (1971), Doll and Peto (1976), and the Surgeon-General of the United States (1979) about the lethality of smoking are precipitate and unwarranted" (p. 102).

In addition to the uncertain state of the death certificate diagnosis, there is another serious directional error in the ascertainment of number of cigarettes smoked. In one of the as yet unpublished Grossarth-Maticek & Eysenck studies, we looked at the accuracy of such statements, better ways of getting accurate statements, and directionality of errors. In the first study we had probands estimate the number of cigarettes smoked; we also had close relatives (usually the spouse) make an analogous estimate. Finally, we got probands to keep a 7-day journal, noting down each cigarette smoked, and the occasion. We found for 136 participants that the own estimate was 12 cigarettes per day. Relatives estimated 18; the journal disclosed 19! In other words, there was a 50% underestimate

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in the proband's own estimate.

In this study a personality inventory, to be described later on, was given after the estimate was made. We put forward the hypothesis that if the inventory was administered first, it would make the proband more likely to give truthful answers. In the matched group of 136 smoking, the three estimates agreed very well - own estimate 17, relative's estimate 16, journal record 18. In our own work, to be described presently, this second method has already been followed.

This degree of inaccuracy is particularly troublesome if it is directional, i.e. if cancer-prone probands were to over-estimate, not-prone probands to under-estimate the number of cigerattes smoked. In a group of 128 cancer-prone probands, ascertained on the basis of a personality inventory as described in a later section, the self-estimation averaged 17, relative's estimation averaged 16, and the journal averaged 15! The other personality types investigated showed under-estimations of between 2 and 18 cigarettes per day, instead of the over-estimation of 2 cigarettes of the cancer-prone probands. This tendency, in general, would greatly exaggerate the statistical correlation between cancer and smoking. Clearly careful experimenters would look at sources of error of this kind, and try to eliminate them; this has not happened in the great majority of studies examined.

We have devoted a considerable amount of space to a discussion of the reliability of the data, and possible biases in the data, because all conclusions in science are absolutely dependent on the quality of the data. When these are as poor as those used by epidemiologists to establish a relationship between smoking and cancer, and smoking and coronary heart disease, then a detailed demonstration of the unreliability and invalidity of the data is imperative. It is noteworthy that those who maintain the "orthodox" view seldom argue

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the case; they accept faulty data without any query, and without answering the critics who draw attention to these fundamental faults.

Another vital criticism of the orthodox view relates to an argument in the U.S. Surgeon-General's report to the effect that: "The relative risk ratio measures the strength of an association and provides an evaluation of the importance of that factor in the production of a disease" (p.17). Such a statement contravenes the logic of epidemiological enquiry and takes for granted that which is to be proved; clearly the risk ratio only provides an evaluation of the importance of the factor and the production of the disease once it has been proved that there is a causal relationship! The strength and consistency of the association cannot be used to prove a causal relationship. However, the absence of a consistency in the strength of the association can certainly be used to throw doubt on the causal implications. From the hypothesis of the universal causal effects of smoking or lung cancer, similar or identical risk ratios should be found, say, in Oriental and Caucasian populations. This, however, is not so (Eysenck, 1980, 1986).

Mortality risks in the dominantly Caucasian populations cluster around an average mortality rate of about 10, ranging from 7.0 to 14.2. Values in Mongoloid populations, however, are very different. In Japan, the value is 3.8; for Chinese residents in Singapore it is 3.8 also, McLennan et al., (1977). In Northern Thailand a value of 1.6 has been reported by Simarak et al., (1977), i.e. not significantly different from unity. Henderson (1979) has reported a risk ratio of 1.57 from Mainland China. For women, the incidence of lung cancer in the Chinese in Hong Kong was reported as only 1.74 by Chan et al., (1979). In Hawaii, a relative risk ratio of 10.5, 4.9 and 1.8 respectively were found for women of Hawaiian, Japanese and

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Chinese origin; this aligns the Hawaiian women with the Caucasian mortality ratios, and contrasts them with the Japanese and Chinese women studied. It is difficult to account for these very large differences in mortality ratios between Caucasians and Oriental groups in terms of the orthodox view; it is much more natural to appeal to genetic causes in this context.

Many other facts have been adduced to support this view (Eysenck (1960, 1976). There is for instance the important work of Belcher (1971), who has reported on worldwide differences in the sex-ratio of bronchial carcinoma. The ratio of men affected, as compared with women, varies widely from one part of the world to another. In Nigeria, for instance, the incidence is actually higher among the women than among the men, whereas in Holland it is over 13 times as high in men as compared with women. There is no relationship between the sex ratio and the total tobacco consumption in different countries, nor is the different age structure of the different populations responsible. Belcher concludes that "there is a genetic factor in the aetiology of bronchial carcinoma" (p.220). All these data are not interpretable in terms of the orthodox view, and throw much doubt on its value in interpreting the observed facts.

Another argument made much use of by the U.S. Surgeon-General and the Royal College of Physicians is an alleged 'dose-response' relationship. As the Surgeon General's report states: "Important to the strength as well as to the coherence of the association, is the presence of the dosage-response phenomenon in which a positive gradient between the degree of exposure to the agent and incidence or mortality rates of the disease can be demonstrated." (p. 17.)

However, such a dose-response relationship would also be predicted from other hypotheses, as Burch (1983) has pointed out:

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"To take the simplest postulates, smokers can be divided into two categories, social and habituated. Social smokers tend to be light smokers and could quit readily; habituated, genetically-predisposed smokers, tend to be heavy smokers. Hence, in any group of light smokers, social smokers will predominate and the association with lung cancer will be relatively weak; in any group of heavy smokers, habituated, genetically-predisposed smokers will predominate and the association with lung cancer will be strong. An apparent 'dose-response' relation will be observed. (p. 826.)

The causal hypothesis, in its pure form, would predict the same response from the same "dose" in different populations; the genetic hypothesis, which assumes that the association between smoking and lung cancer depends on the strength of the associations between patients' presenting genotypes, rather than on smoking levels, would predict some correlations, though not necessarily a very high one, between national mortality and national smoking levels. The observed relationship between national mortality from lung cancer and national cigarette consumption is not very strong. As an example of discordance, we may take the age-standardized mortality from lung cancer in Finnish men in 1960-61, which was about double that in U.S. white males, whereas cigarette consumption in 1950 in Finland was about half that in the United States (Burch, 1976). There are many other anomalies of this kind, as the perusal of the report will show; Burch (1983, p. 826) has pointed out: "The pure causal hypothesis might, by this test alone, appear to be untenable. The existence of the weak correlation between national rates of mortality and smoking is consistent with the causal component but it is also consistent with the pure constitutional hypothesis and no causal action."

Passey (1962) has thrown doubt on the existence of a proper dose-

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response relationship within a given population. As he points out: "Nowhere has it been claimed that the heavy smoker is stricken with cancer earlier than the light smoker. If lung cancer in smokers is the result of direct carcinogenic action, one would certainly expect this to happen; for experiment has shown beyond question that a potent carcinogen induces tumours early" (p. 110). Passey next examined the smoking history of 499 men with lung cancer, grouping the cases according to the number of cigarettes smoked. He gives a table which shows "that the amount smoked makes no appreciable difference to the mean age at which the person first reported to the clinic. The light smoker is afflicted with lung cancer at the same age as a heavy smoker. This is a surprising observation. The mean age at which smoking was started was 17; the average amount smoked daily was 23 cigarettes; the mean age at which the patient presented at the clinic was 57 years...the mean smoking period was some 40 years" (p. 109). Nor was it true, as might be said, that the youngest of these patients with lung cancer might have smoked particularly heavily, and that the eldest had survived because they were specially moderate smokers: "The amount smoked daily by old and young is not dissimilar. Yet the oldest patient had smoked for some 50 years longer than the youngest patient - this represents well over a quarter of a million more cigarettes. These figures suggest that there is no relation between the amount smoked daily and the age of onset of lung cancer" (p. 111. See also Herrold, 1972).

Pike and Doll (1965) replicated Passey's findings from their sample of British doctors. They concluded that: "Neither the amount smoked nor the age of starting made any substantial difference to the average age of onset of the disease" (p. 667), and these conclusions were also found valid for the "life-span" average under the conditions

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in which lung cancer is produced in man.

Last but not least in discussing the strength of the association, we must consider the paradox presented by mortality ratios as related to degree of inhalation. On the orthodox view it would be expected that inhalation would give much higher mortality ratios, for equal amounts smoked, than would lack of inhalation. Fisher (1959) analysed retrospective data of disease by daily rate of smoking; inhalers had a paradoxically lower risk of lung cancer than non-inhalers. Doll and Peto (1976), in a twenty-year follow-up of British male doctors, standardized for age and amount smoked (in nine groups) found overall that the risk of lung cancer in inhalers was 84% of that of non-inhalers. A thorough discussion of the evidence is given by Eysenck (1980).

The latest study along these lines (Higgenbottam et al., 1982), reporting on 18,403 male civil servants, found that "lung cancer rates were higher overall for (non-inhalers), particularly in heavy smokers" (p. 113). They attempt an ex posteriori explanation, but this is highly speculative and has no basis in empirical studies. Furthermore, it would not allow us to predict that coronary deaths were more common among inhalers, as also found by Higgenbottam. The facts as they stand are clearly an embarrassing anomaly for adherents of the orthodox view, and difficult to reconcile with it. The absence of the anticipated relationship between inhalation and lung cancer must, as Fisher already pointed out in his original paper, be a severe blow to the orthodox view, but remarkably little effort seems to have been made to accommodate the finding and attempt to explain it along causal lines.

Much is made by adherents of the orthodox view of the temporal congruence between increases in smoking and increases in lung cancer.

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We have already examined the alleged increase in the incidence of lung cancer, and found that the evidence does not really support any such increase, but rather suggests that changes in diagnostic methods enable us to identify lung cancer more readily (and perhaps too readily, considering the overdiagnosis to which we have alluded!).

Of particular interest is the temporary relationship observed in the differential patterns for males and females. In the United Kingdom there occurred a sharp increase in cigarette consumption by women about thirty years after that which occurred in males. However, Burch (1976), 1983) has shown that: "When rise in recorded mortality from lung cancer is studied in detail, it is seen that the temporal pattern of increments, from one five-year period to the next, is remarkably synchronous in the two sexes from the beginning of the century to 1955 and then from 1965 onwards. It follows that the main causes of the recorded increases in both sexes were also synchronous in both sexes and therefore could not have been cigarette smoking" (1983, p. 828). Thus what is claimed to be one of the strongest proofs for the received view turns out, on detailed examination, to be a strong argument against that view.

One other example of the numerous inconsistencies in the way of temporal relationships must suffice. Guberan (1979) has demonstrated a surprising decline of cardiovascular mortalities in Switzerland from 1951 to 1976, in spite of <u>increasing</u> smoking by women and roughly stationary smoking rates in men. There was also a 20% rise in consumption of animal fats; yet age-standardized death rates for all diseases of the circulatory system decreased by 22% in males and by 43% in females. These results are difficult to assimilate for adherents of the orthodox view.

As an example of the complexity of the issues encountered by

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epidemiologists, consider laryngeal cancer. Rothman et al. (1980) demonstrate a linear regression of age-standardized mortality from laryngeal cancer on number of cigarettes smoked daily (Fig. 3, p. 201), and Shell (1972) found a similar correlation. Yet Curwen et al. (1954) and MacMichael (1978) failed to discover the expected dramatic upsurge of such cancer in recent years, to parallel the (alleged) dramatic increase in lung cancer! Perhaps methods of diagnosis for laryngeal cancer have not shown the great improvement that methods of diagnosis for lung cancer have enjoyed.

We must conclude that the study of the temporary relationship of the association between cigarette smoking and cancer is vitiated by the poor quality of the data, but as far as that goes it does not offer any support for the orthodox view.

We have examined some of the criticisms of the methodology and the data used to establish the orthodox view; a much more detailed account has been given elsewhere (Eysenck, 1980, 1986). We have not yet extended the review to the issue of "passive" smoking; the notion that passive smoking can cause disease has been criticized on methodological and statistical grounds by Aviado (1986), and there is nothing in the recent literature to alter his verdict that "there is no substantial evidence to support the view that exposure to environmental tobacco smoking presents a significant health hazard to the non-smoker. After a detailed consideration of the circulatory and respiratory diseases studies, it is concluded that there are inadequate data on which to base the conclusion that exposure to environmental tobacco smoke causes such diseases. Consequently, in this author's view, non-smokers should not use claims of adverse health effects as justification for not interacting with smokers in society". (p. 8.)

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Is this conclusion faulted by more recent evidence? The report of the National Health and Medical Research Council of Australia (1987) is not intemperate in its conclusions. They note that "in several important areas, there is insufficient scientific evidence yet available. In particular: (1) the effect on lung function of acute exposure to passive smoke in healthy individuals appears not to be substantial nor is the evidence consistent; (2) few data are available regarding the effects upon both the upper and lower respiratory tracts of chronic passive smoking in healthy individuals; and (3) there are no data on the effects of passive smoking during childhood on subsequent lung function in adulthood." (p.44). With regard to lung cancer they say that there is mounting epidemiological evidence that passive smoking may increase the risk of occurrence of lung cancer but they note "limitations in the amount of data available", and "research difficulties in making satisfactory estimations of individual exposure"; all this is perfectly reasonable. They also note that "there is very limited evidence available about the cardiovascular effects of passive smoking." (p.44.) The Council finally "acknowledge that further research is necessary to confirm and elaborate the effects of passive smoking upon health."(p.45)

The report of the U.S. Surgeon General (1989) is much more definite. Thus it is asserted that "it is certain that a substantial proportion of the lung cancers that occur in non-smokers are due to ETS (environmental tobacco smoke) exposure"; it is admitted, though, that "more complete data on the dose and variability of smoke exposure in the non-smoking U.S. population will be needed before a quantitative estimate of the number of such cancers can be made". (p.X.) Regarding the relationship between ETS and cancers other than lung cancer and cardiovascular disease, it is stated that "further

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research in these areas will be required to determine whether an association exists between ETS exposure and an increased risk of developing those diseases". (p.XI.)

On what sort of evidence is all this based? As the Australian report states, the conclusions depend on "observing empirical associations between reported individual smoking habits and the occurrence of cancer. Such observations are made in either cohort (prospective) studies or case-control (retrospective) studies." (p.27.) There are many difficulties and problematical assumptions involved in this process. As the authors of the U.S. Surgeon General's report (1989) point out, "the quantification of the risks associated with involuntary smoking ... is dependent on a number of factors which only a limited amount of data are currently available." (p.96.) The first such factor noted is the absolute magnitude of the lung cancer risk associated with involuntary smoking; the studies reported in the book do not contain a zero-exposure group." The magnitude of the difference in tobacco smoke exposure between groups identified by spousal smoking habits may vary from study to study; this variation may partially explain the differences in risk estimates among the studies." (p.96.)

The second factor noted is the lack of suitable data on the dose and distribution of exposure to ETS in the population. "The studies that have been performed have attempted to identify groups with different exposures, but little is known about the magnitude of the exposures that occur in different segments of the U.S. population or about the variability of exposure with time of day or seasons of the year." (p.96). In other words, fundamental and basic facts are not known.

Of 13 studies reported, 6 give insignificant results; the fact

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that so few give statistically significant results makes the report plead for the use of one-tail tests, in order to boost significance by inadmissible means - we are to assume what we are trying to prove! They argue that "the lack of statistical significance in all studies should not invalidate the positive significant associations for involuntary smoking that have been observed." (p. 97.) But such a conclusion of course depends on the adequacy of the methodology of these studies.(1)

The report notes several "serious criticisms", such as the misclassification of the active smoking status of the subjects, "which can produce an apparent increased risk with involuntary smoking." (p. 101.) It is also noted that "it is likely to result in differential misclassification because spouses tend to have similar smoking habits." (p. 101.) Misclassification of the lung as the primary site and the lack of pathological confirmation are repeated concerns." (p. 101.) "Misclassification of exposure to ETS cannot be dismissed, since an index based solely on the smoking habits of a current spouse may not be indicative of past exposure, cumulative exposure, or the relevant dose to the respiratory tract." (p. 101.) It is admitted that "the magnitude of risks associated with involuntary smoking exposure is uncertain." (p.101.) These are some of the criticisms voiced in the report; it does not seem reasonable to base any far-reaching conclusions on such doubtful data.

But worse still, the authors do not consider at all many of the cogent criticisms made of the "smoking causes cancer" literature, which apply with special force to ETS exposure. No attention is paid to the synergistic interaction of risk factors, or the impermissible use of the concept of "cause" in the context of complex inter-relations. Very doubtful and admittedly unquantifiable risk

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Footnote, p. 61.

(1) It also depends crucially on the validity of the statistics employed. The most widely quoted results favouring an association between passive smoking and lung cancer are those of Hirayama (1981a) and Trichopolous et al. (1981). As regards the first of these, Mantel (1981) provided a detailed criticism of the statistics, pointing out serious errors and misinterpretations, to which Hirayama (1981b) failed to respond properly, but added some new information. Lee (1981) further showed that Hirayama's 11 printed confidence intervals were all in error by factors of up to 1000%, errors later acknowledged by Hirayama's work, and makes one wonder how anyone can still cite it as evidence of the evils of passive smoking, as the Surgeon-General's Report continues to do.

The work of Trichopolous et al. (1981, 1983) has also been shown to be seriously faulty, as pointed out by Heller (1983). Trichopolous (1984) excused this as a "typing error" - a rather casual response to a most serious criticism of his principal conclusions! These matters have been misreported in the Surgeon-General's (1986) report and in the Australian NHMRC report (1987), both of which fail to acknowledge the serious and indeed fatal errors contained in the Hiroyama and Trichopolous studies. One cannot fail to note the acceptance by the authors of these reports of badly compromised data in support of their claims, and the refusal to cite well-established data hostile to these claims. The whole affair reflects poorly on both the authors of the original studies, and on the compilers of the official reports.

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ratios become "substantial proportions" in the summary of the Surgeon-General. No allowance is made for other risk factors, like drinking, air pollution, stress, diet, etc., whether correlated with smoking or not. To give but one simple example, if people smoke in part because they are stressed, then it seems likely that their spouses will also be stressed; as we shall see, stress is a strong risk factor for lung cancer, and may mediate the (at best weak) association between ETS exposure and lung cancer. Hundreds of such alternative possibilities suggest themselves, but none are mentioned or investigated by the authors of the report. Science advances by a consideration of plausible alternative hypotheses, not by complete disregard of explanations which may conflict with assumed dogma.

We must conclude that admittedly there is little if any evidence to link cancer or CHD with ETS exposure. For lung cancer, there are some published studies which produce evidence of a statistically significant correlation (6 out of a total of 13), with a majority failing to produce such a correlation. The report recognizes serious criticisms of the work done, criticisms which would seem to invalidate any positive conclusions. The report fails to deal with even more serious criticisms, including the impropriety of interpreting (doubtful) statistical association in causal terms. We must conclude that Aviado's (1986) summing-up has not been overturned by the most recent evidence, and that proof is still lacking concerning the adverse effects of passive smoking in cancer and CHD.

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(5) The Causes of Smoking: Needs or Addiction?

An important part of the orthodox view is that smoking is an addiction, and hence that nicotine joins the addictive drugs like heroin, LSD, etc. A recent report of the Surgeon General (1988), with the title of "Nicotine Addiction", contains the following major conclusions:

1. Cigarettes and other forms of tobacco are addicting.
2. Nicotine is a drug in tobacco that causes addiction.
3. The pharmacologic and behavioural processes that determine tobacco addiction are similar to those that determine addiction to drugs such as heroin and cocaine. (p. 9.)

Is it true that nicotine is an addictive drug, or is an alternative hypothesis more likely, namely that nicotine has effects on human beings which fulfil certain needs, just as food satisfies the need caused by hunger and drink serves the need caused by thirst? This is an important debate, particularly as it will be seen to lead into the question of personality as related to smoking, and smoking-related diseases. A detailed account of the arguments has been given by Warburton (1985), who discusses the many meanings of the term "addiction", and also looks at the question raised by the Surgeon General in a detailed examination of the evidence (Warburton, 1989). As Warburton points out, originally the term "addiction" was used for any strong inclination for any kind of conduct, good or bad. It is only recently that certain patterns of drug use have been labelled as "addictions", and today, "addiction" is often used to imply an undesirable, and usually an illegal, use of drugs. In the same way

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the noun "addict" has lost its denotative meaning of people engaged in certain habits and has become a stigmatizing label, implying someone with a disease.

Alcoholics and drug users in the past were regarded as morally depraved, but by the end of the 19th Century they were regarded as diseased (Berridge and Edwards, 1987). The disease concept of drug use carries with it the implication that the "addict" has some "physiological addiction mechanism", so that the person is at the mercy of physiological cravings. Similarly, relapse is a symptom of the re-emerging disease. Other authors regard drug use as a type of mental disease, a lack of willpower, thus linking notions of moral, psychological and physiological pathology in the concept of addiction.

As Warburton points out, the U.S. Surgeon-General (1988) has produced lists of criteria for defining nicotine use as an "addiction" which depend on argument by analogy. Such arguments are dangerous; they may be used to suggest a conclusion, but they cannot establish it. Warburton argues that the U.S. Surgeon-General has ignored the discrepancies in his argument in his enthusiasm to find criteria to compare nicotine users with heroin and cocaine users. Three primary criteria are suggested by the U.S. Surgeon-General. The first of these is that the drug has psychoactive effects. This is a novel criterion, not normally used in this field of substance use; it is supported by the U.S. Surgeon-General by stating that "to distinguish drug dependence from habitual behaviours not involving drugs, it must be demonstrated that a drug with psychoactive (mood altering) effects in the brain enters the blood-stream" (p. 7-8.) As Warburton points out this criterion is trivial. Entering the blood-stream does not define psychoactivity; the important issue for the Surgeon General's argument is whether the actions of nicotine are like those of cocaine

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and the opiates. Certainly both heroin, cocaine and nicotine are psychoactive, but they are very different in their effects. Heroin induces euphoria, but it also impairs performance, and cocaine impairs judgement; nicotine, on the other hand, improves performance, renders the user more alert and increases his efficiency of performance and reduces anxiety (Warburton, Revell and Walters, 1988). As Pomerleau and Pomerleau (1984) state: "In contrast to drugs of abuse, nicotine from smoking is not only compatible with work but actually facilitates performance of certain kinds of tasks". Thus, in terms of psychoactive drug use, nicotine has a behavioural mode of action which is quite different from heroin and cocaine.

The second major criterion adduced by the U.S. Surgeon General relates to drug-reinforced behaviour, which means "the pharmacological activity of the drug is sufficiently rewarding to maintain self-administration". With drugs such as heroin and cocaine, rats and monkeys can be readily trained to press a lever to obtain an injection, but this is not so with nicotine. It is difficult to train monkeys to lever-press for nicotine, and the pattern of administration bears no relation to human smoking.

The whole argument seems beside the point. According to the report: "Addicting drugs often provide...benefit or otherwise useful effect; these effects may also contribute to the compulsive nature of drug use." (p. 250.) What this statement seems to mean is that if something is beneficial, it can be addicting! This would suggest that food and sex are "addictive"!

The third major criterion is highly-controlled or compulsive use. In the U.S. Surgeon General's report it is stated that: "Highly-controlled or compulsive use indicates that drug-seeking and drug-taking behaviour is driven by strong, often irresistible urges". (p.

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7.)

As Warburton points out "this degree of "compulsion" hardly seems to apply to nicotine. Many smokers have patterns of smoking behaviour by which they smoke at work, but not at home, and vice versa. Many refrain from smoking for relatively long periods, for practical or religious reasons, without apparently experiencing any hardship, e.g. coal miners who cannot smoke at the pit face and Orthodox Jews who do not smoke on the Sabbath. As Ashton and Stepney (1982) state about these smokers: "The rationale for labelling them as addicts is not convincing". In a similar way, Warburton examines secondary criteria cited by the U.S. Surgeon-General, i.e. stereotypic patterns of use, recurrent drug cravings, relapse following abstinence, and induced death by its harmful effects. There is also a set of tertiary criteria, namely that of pleasant or euphoric effect, tolerance, and physical dependence. None of these secondary or tertiary criteria emerge with credit from Warburton's critique, but in view of the widespread belief that physical dependence uniquely defines addiction, it may be worthwhile to consider his critique. As he points out, the existence of physical dependence is an inference made from the abstinence syndrome that occurs when a chronically-administered drug is discontinued. Certainly, there are marked, stereotyped symptoms that occur after giving up heroin or alcohol. However, the reported changes after smoking abstinence differ widely from one individual to another and are not present at all in 25% of people giving up smoking. As the Diagnostic and Statistical Manual 3-III observes, discussing nicotine: "In any given case, it is difficult to distinguish a withdrawal effect from the emergence of psychological traits that were suppressed, controlled or altered by the effects of nicotine or from a behavioural reaction (e.g. frustration) to the loss of the

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reinforcer." (p. 150.)

We may conclude from Warburton's discussion that the term "addiction" is difficult or impossible to define, and certainly has no agreed scientific meaning. The criteria used by the Surgeon General are rather arbitrary, at times trivial, and certainly fail to nail down cigarette smoking as an addiction in any meaningful sense. How then do we explain its prevalence, and the difficulties many people have in giving it up, in spite of the propagandist efforts to suggest that very serious health consequences follow from its continued use?

An alternative way of looking at the situation was suggested by Eysenck (1973). The suggestion is that different people smoke for a variety of reasons, depending on needs in relation to personality, so that they are not addicted in any meaningful sense, but continue to smoke because they derive certain benefits from smoking, just as they do from eating, drinking, and many other activities. This possibility was first raised by Eysenck et al., (1960) in a paper suggesting that perhaps extraverted people smoked because they were bored, and wanted to raise their cortical level of arousal, while neurotic people smoked in order to reduce their tensions and anxieties. While apparently contradictory, both these results can be achieved by varying the amount of nicotine taken into the blood-stream, nicotine affects apparently being bi-phasic (Eysenck, 1980). This theory was developed and strengthened by various empirical investigations in later publications (Eysenck, 1973; Eysenck and O'Connor, 1979; Eysenck, 1980).

A typical test of the hypothesis that smoking correlates with extraversion, and associated personality traits diagnostic of sensation-seeking, has been reported by Knorring & Oreland (1985). In a study of an unselected series of 1129 18-year-old men from the

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general Swedish population, they found that regular smokers were extraverted, and sensation-seeking, easily bored, and with a strong tendency to avoid monotony. These men also had a low level of platelet monoamine oxidase, known to be related to sensation-seeking, impulsivity and extraversion. Ex-smokers had personality traits and platelet monoamine oxidase of the same magnitude as non-smokers, another indication that smokers and ex-smokers are different in many more ways than just giving up or not giving up smoking.

A study by Frith (1971) provided important evidence to show by an analysis of occasions when people smoked cigarettes that indeed they fell into two clearly marked groups, one class of situations being boring and producing a need to raise cortical arousal, the other being characterized by stress of one kind or another, suggesting a need for relaxation. There is now a very large literature on this and related theories, reviewed in detail by Spielberger (1986), and it would not be appropriate to review it again here. By and large other authors have replicated the original studies, but have suggested additional reasons for smoking. Particularly important has been the Tomkins (1968) Affect Control Model, which distinguishes four general types of smoking behaviour: (1) positive affect smoking; (2) negative affect smoking; (3) addictive smoking; and (4) habitual smoking.

In negative affect or sedative smoking, according to the theory, an individual smokes to reduce unpleasant feelings of distress, anger, fear, shame, contempt, or any combination of these primary affects. In contrast, positive affect smokers generally smoke when they feel good, and many never smoke while experiencing negative affect. The addictive type smokers, according to Tomkins, smoke both to stimulate positive affect and to reduce negative affect. For the habitual smoker, on the other hand, smoking has become an automatic habit, and

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although habitual smokers may have originally smoked to enhance positive affect, reduce negative affect, or both, affect is no longer associated with smoking.

There are other possible causes, such as increasing attention, and reducing drowsiness, etc., but it is not the purpose of this section to given a extensive list of possible causes for smoking, and the needs reduced by smoking. It is sufficient to make the point that smoking does satisfy certain needs of different individuals, depending on their personality, circumstances, etc.

It should be noted that we are talking about the maintenance of the smoking habit, which has been shown to be fairly closely related to these needs, and to have a strong genetic element (Eysenck, 1980). The origins of the smoking habit relate more to peer pressure, have no strong genetic component, and are not necessarily related to the needs which cause the habit to be maintained, once the habit has been acquired.

The value of such an analysis can best be demonstrated by reference to efforts to eliminate the smoking habit. As is well known, traditional methods usually have some effect while the therapy is going on, but once that is finished the habit is quickly re-acquired by most of those who have participated in the therapy. This seems likely to be due to the fact that individual needs still exist, leading to a resumption of smoking, and that the original therapy, being designed for all participants, neglects the individual needs of members of that group. An effort was made to use the conceptions outlined above in improving methods of therapy for smokers by O'Connor and Stravynski (1982). The aim of the study was to validate a situational smoking typology by testing its efficacy in designing reduction strategies. Volunteer smokers were scored on a

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situational smoking questionnaire which allowed smokers to be classified into high- and low-activity groups on the basis of main cravings. High-activity smokers were further classified into those who smoked either under emotional stress, or to aid concentration, whilst low-activity smokers were subdivided into those who smoked to relieve boredom, or to relax. From this situational model of motivation, alternative behavioural strategies tailored to the smoker's specific situational demands were devised, in the hope that these might achieve the same effect as smoking and so aid reduction. Thus smokers who wanted to relieve boredom were taught other methods of doing so, such as playing games, etc. Patients who were in a high state of anxiety or tenseness were taught methods of relaxation in order to reduce the anxiety without involving nicotine.

Smokers were allocated at random to one of three treatment groups. The first was a behavioural substitution group, treated according to the principles outlined above by providing substitute behaviour to take the place of cigarette smoking. The second group received a generalized coverant approach where emphasis was placed on generalized beliefs about smoking effects rather than situational ones; this was a routine procedure in the drug addiction unit at the hospital where the research was done. Finally there was a no-treatment control group, where subjects only self-monitored their smoking over the treatment period. Results of the treatment are shown in Fig. 2. The ordinate shows the mean number of cigarettes smoked per day, the abscissa the progress of the experiment from a baseline over 4 treatment sessions to 2 follow-up sessions, respectively 2 and 8 months after cessation of treatment. The results are quite clear-cut. The control group showed no change. The behavioural group is about twice as successful as the coverant group

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in eliminating the habit. Most important of all, however, is a final follow-up which shows a return to the habit on the part of the members of the coverant group, but a continuation of the quitting behaviour on the part of the members of the behavioural group. Differences are statistically significant between the groups, and indicate the value of the need reduction model.

Fig. 2 here.

These results show fairly clearly that the addictive model is inappropriate for most if not all smokers. People smoke cigarettes because smoking behaviour reduces certain needs, and is thus rewarding. When these needs can be met through alternative behaviours, smoking behaviour rapidly drops and is eliminated. The addiction model is not a suitable one for cigarette smoking, and a continued use of the word "addiction" in relation to smoking behaviour has no scientific validity.

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(6) Personality and Stress as Risk Factors.

Historically, there has been a great deal of speculation about the possible role of personality and stress as risk factors in the causation of cancer and coronary heart disease. For cancer, good summaries will be found in the works of Bammer & Newberry (1981), Cooper (1984), Hager (1986), Levy (1985), and Pohler (1989). For coronary heart disease, the writings of Price (1982) and Steptoe (1981) are relevant, and for stress research in general a book edited by Cooper (1983). Based on research of this kind, there has been a good deal of interest in the possibility of preventing cancer and coronary heart disease by suitable intervention through psychotherapy. (Eylenbosch, Depoorter and Larebeke (1988).

There has also been much interest in the possibility of prolonging life through instilling a "fighting spirit" type of reaction in sufferers from cancer and quite generally in the importance of mental attitudes to survival. The evidence certainly suggests that mental attitudes constitute an important prognostic factor in cancer (Greer, Morris & Pettingale, 1979; Pettingale et al., 1981, 1985; Nelson et al., 1989; Eysenck, 1988; Grossarth-Maticek, 1980.)

Ideas concerning the importance of personality and stress have in recent years been incorporated in a number of theories leading to highly focusssed investigations. The possibility that Type A behaviour might be related to, and predictive of coronary heart disease has received a good deal of attention (Rosenman and Chesney, 1980), but reviews such as those by Friedman and Booth-Kewley (1987) have suggested that only certain traits of the Type A personality, such as anger and aggression, might be related to coronary heart

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disease (Eysenck, 1990). Our own work (Grossarth-Maticek, Eysenck & Vetter, 1988) certainly supports this view.

About the relevance of stress to CHD, there exists a good deal of confirmatory evidence (e.g. Hanson, 1987; Kaplan et al., 1978.) Brindley & Rolland (1989) have recently reviewed the evidence, concluding that "an increased control of metabolism by the 'stress' or counter-regulatory hormones....is a common feature of (CHD) risk factors. Particular emphasis was placed upon the action of the glucocorticoids - (which) can decrease energy expenditure and, together with insulin, promote energy deposition. These observations provide a partial explanation for the metabolic changes that can accompany the risk factors and clarify why they interact in promoting atherosclerosis." (p.459.)

As regards the cancer-prone personality, this has often been described as appeasing, unassertive, overco-operative, overpatient, harmony seeking and conflict avoiding, compliant and defensive (Baltrusch et al., 1988). The two most frequently noted characteristics are (1) suppression of emotional expression, and denial of strong emotional reaction; and (2) failure to cope successfully with stress, and the reaction of giving up, linked with feelings of hopelessness and helplessness (Eysenck, 1985; Baltrusch, Stengel & Waltz, 1988). This type has sometimes been called "Type C", to distinguish it from the coronary heart disease-prone Type A, and the healthy Type B. (Temoshok, 1987.)

Many studies have given support to the notion of a "cancer-prone" type, but most of these have been studies comparing individuals suffering from cancer with controls of one kind or another (Eysenck, 1985). Three major prospective studies were mounted to overcome the possibility that the cancer might have caused differences in

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personality, rather than that personality and stress were risk factors for cancer. These three studies have been described in detail by Grossarth-Maticek, Eysenck & Vetter (1988), and we will only quote the major results. The first of these studies was carried out in a small country town in Yugoslavia, where every second household was studied, and the oldest inhabitant used as proband. (There was also an additional small sample of highly stressed people, and occasionally when the oldest inhabitant was a female, Yugoslav macho attitudes made it necessary to take into the sample the oldest male. These deviations from the research plan had the effect of worsening the outcome, rather than improving it, but the figures given below are for the total sample.)

The other two studies were carried out in Heidelberg, and used in the first instance a normal, fairly random sample, with certain age and sex limitations imposed. The second Heidelberg sample was a stressed sample; its members were nominated by members of the normal Heidelberg sample as being highly stressed; they came largely from friends and relatives of members of the first sample.

Members of these samples were interviewed and given a personality/stress questionnaire; they also gave information concerning their smoking and drinking habits; and blood pressure and blood cholesterol were investigated, in order to have some medical information relevant to these possible risk factors.

The personality/stress interviews and questionnaires were used to assign each proband to one of four types. Type 1 was believed to be cancer-prone, showing the characteristics outlined above. Type 2 was believed to be coronary heart disease-prone, again showing a set of characteristics quite different from those of the cancer-prone type. Type 1, in brief, is characterized by under-stimulation; persons of

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this type show a permanent tendency to regard an emotionally highly valued object as the most important condition for their wellbeing and happiness. The stress produced by the continued withdrawal or absence of this object is experienced as an emotionally traumatic event. Type 1 individuals fail to distance themselves from the object and remain dependent upon it. Thus individuals of this type do not achieve success in reaching the object, and remain distant and isolated from this highly valued and emotionally important object. Great stress is produced by the failure to achieve nearness to the highly valued person, success in a highly valued occupation, or whatever.

Persons of Type 2 (CHD-prone) rather show <u>over-arousal</u>; they show a continued tendency to regard an emotionally highly important object as the most important cause for their particular distress and unhappiness. Rejection by the object, (if a person), or failure to reach it (as in the case of occupational success) is experienced as an emotional trauma, but persons of this type fail to achieve disengagement from the object; rather they feel more and more helplessly dependent on the object. Thus persons of this type remain in constant contact with these negatively valued and emotionally disturbing people and situations, and fail to distance themselves and free themselves from dependence on the disturbing object, reacting with anger (open or suppressed) and aggression.

There is a third type, Type 3, characterized by ambivalence. This type shows a tendency to shift from the typical reaction of Type 1 to the typical reaction of Type 2, and back again. Members show a permanent tendency to regard a highly valued object alternately as the most important condition for his own wellbeing, and is the main cause for their own unhappiness. In individuals of this type, we have an

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alternation of feelings of hopelessness/helplessness and of anger/aggression. Possibly because of this alternation of quite different reaction types, this particular type of proband seems to be relatively safe from both cancer and coronary heart disease.

Persons of Type 4 are characterized by personal autonomy, and in some ways resemble Type B of the Friedman-Rosenman typology, or to the "hardy" personality of Allred & Smith (1989). For persons of this type there is a strong tendency to regard their own autonomy, and the autonomy of the persons with whom they wish to be in contact, as the most important condition for their own wellbeing and happiness. This enables them to experience realistically the approach or avoidance behaviour of the object of their desires, and thus enables them to accept the autonomy of the object. An inventory to determine which type a proband belongs to has been reproduced in the paper by Grossarth-Maticek, Eysenck & Vetter (1988).

Table 4 shows deaths, and causes of deaths, from various diseases by type of personality in the Yugoslav sample. The crucial figures are the percentage of deaths from cancer in Type 1 (46.2%), and the percentage of deaths from coronary heart disease in Type 2 (29.2%). The figures for both are obviously much lower for Types 3 and 4, and the data give substance to the view that personality and stress can be used to predict deaths from cancer and coronary heart disease. It will also be clear that Type 3 has a high proportion of deaths from other causes, whereas Type 4 has much the largest percentage of probands still alive.

Table 4 here.

Table 5 shows deaths from various diseases by types of

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personality in the Heidelberg normal sample. Here the number of deaths is very much smaller, because the sample is younger than was true of the Yugoslav sample (the average age of the Yugoslav sample was 62 years, that of the Heidelberg normal and Heidelberg stressed sample was 50 years of age.) Clearly, cancer and coronary heart disease are diseases of old age, and the ten year difference in age makes a considerable difference to the number of deaths expected. Nevertheless, the figures clearly show again a relationship between cancer and Type 1, and coronary heart disease and Type 2.

Table 5 here.

Table 6 shows deaths from various diseases by type of personality in the Heidelberg stressed sample. Here the number of deaths is much closer to that in the Yugoslav study, in spite of the difference of ten years in age; as the two Heidelberg samples are very similar in all other respects, it seems reasonable to attribute this larger numbers of deaths to the stress experienced by this group. In the Heidelberg normal sample, 88.6% were still alive at the end of this ten year follow-up; in the Heidelberg stressed sample, only 54.3% were still alive. This difference is one of the best pieces of evidence for the importance of stress in causing death that exists in the literature.

Table 6 here

The data can be inspected more directly in the form of Figures 3, 4 and 5, which show clearly how close is the relation between personality type and disease.

Figs. 3, 4 and 5 here

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We must now consider the importance of smoking for the type-cancer relationship. Table 7 shows a number of cancer deaths, other deaths and total deaths for non-smokers and smokers of Type 1, as compared with individuals of the other three types. Among non-smokers, as expected, there are very few deaths from lung cancer, but of the 13 that occur, 10 occur in persons of Type 1. For smokers, there are 74 deaths, only 6 of which occur in persons other than Type 1. These results give rise to an association between Type 1 and lung cancer of P = 0.0001 for both the samples considered when a correction has been made for differences in smoking habits according to the Mantel-Haenszel (1959) formula. It is clear that quite independent of smoking, individuals of Type 1 are cancer-prone, as compared with individuals of Type 2, 3 and 4. (See also Grossarth-Maticek, Eysenck & Vetter, 1988.)[1]

Table 7 here.

This table also makes clear that there is a synergistic interaction between smoking and typology. The only group which has a high proportion of deaths from lung cancer is that of smokers of Type 1; smokers not of Type 1, and non-smokers either of Type 1 or of the other types have negligible rates of cancer deaths. Of the two factors, smoking and personality, personality seems to be the stronger. Of 735 smokers not of Type 1, 6 only were found to have died of lung cancer; this figure is not very different from 3 non-smokers not of Type 1 who died out of the 850 individuals who were non-smokers. Clearly smoking appears to represent a danger to health as far as lung cancer is concerned only for individuals of Type 1.

The data may deserve a slightly more formal analysis, following

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Footnote, p. 78.

1. There are several explicit or implicit replications of these studies, showing similar relationships. A review of earlier studies has been given by Eysenck (1985). More recent studies are those of Kune et al. (in press), Quander-Blaznik (in press), Beek (no date), and Wirsching et al. (1981). Of particular interest is the work of Baalen & de Vries (1987), who showed that in patients with extensive metastases who recovered without operations or chemotherapy, all had personalities resembling those of Type 4.

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the traditional methods of epidemiology (Perkins, 1989). The background factor for the two populations (Yugoslav and Heidelberg stressed) taken together is .35% for lung cancer mortality (N=850). For personality in non-smokers it is 2.89%, giving an excess of 2.54% (2.89% - .35%), which may be called the personality effect. For smoking in personality other than Type 1 the effect is .45% (.80% - .35%), i.e. about a fifth of that of personality. The combined effect of smoking and personality is 15.21% (15.56% - .35), which is 5 times the effect expected from simple addition of the smoking and personality effects (.45% + 2.54% = 2.99%). Thus synergism produces a 500% increase in cancer mortality from smoking and personality.

This calculation is taken over 2,374 people, giving 77 cases of lung cancer mortality; the numbers are clearly not large enough to take the resulting calculations as anything but a very rough and ready guideline. Also it may be objected that the calculation brings together two rather unlike populations (Yugoslav and German), differing in age and stress. However, both groups give similar results when analysed independently, and hence may not be too dissimilar for the purpose of analysis. (The Heidelberg normal group had too few cases of lung cancer to be included.)

We have carried out similar analyses for other risk factors (blood pressure, blood cholesterol), and compared these with smoking as a risk factor. Details and figures are given elsewhere (Grossarth-Maticek, Eysenck & Vetter, 1988). These analyses were carried out for all three samples, i.e. the Yugoslav, the Heidelberg normal and the Heidelberg stressed sample. The results are quite similar, no matter which dependent variable, which organic variable and which place of investigation is considered. Table 8 show the results.

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Table 8 here.

(1) The organic variable has different relevance for mortality depending on the psychosocial type. Its relevance is greatest with that type which itself has the greatest specific mortality, i.e. Type 1 for cancer, and Type 2 for coronary heart disease. In other words, the psychosocial types are relevant, not only for mortality, but in a similar way for sensitivity to organic risk factors.

(2) The psychosocial types do show differences with respect to the organic variables, but these differences cannot explain away the relevance of the types for mortality; according to the figures for mortality, type-specific mortality differences when adjusted for differences of the organic variables are still highly significant.

These data suggest several conclusions. Psychosocial variables, and particularly personality type and stress, are important in mediating deaths from cancer and coronary heart disease. These personality variables are more influencial than physical factors like smoking, blood pressure, and cholesterol, in the ratio of roughly 6-1.

Finally, personality and physical factors interact in a synergistic fashion. These are important findings for any attempt to prevent deaths from cancer and coronary heart disease.

The findings that risk factors in cancer and coronary heart disease act synergistically, not by simple addition, is so important that these findings may be amplified by two studies not yet published. One of these is summarized in Table 9.

In this table, we are dealing with the results of a study in which we compare death rates of probands having 1, and 2, and 3, or all 4 of four different risk factors. The risk factors were (1) smoking (more than 20 cigarettes per diem, for over 10 years), (2)

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heredity (at least one first-degree relative suffering from or died of lung cancer), (3) chronic bronchitis, and (4) stress, i.e. probands of Type 1 or 2. Not all combinations of risk factors could be found in sufficient numbers, but the data show very clearly the synergistic effects of multiplying risks.

Table 9 here.

It will be seen that in these probands, who were on average between 51 and 54 years old at the beginning of the study, 13 years later none had died of lung cancer of those who only showed one risk factor. Of those showing 2 risk factors, only about 1% died of lung cancer. Combinations of 3 risk factors showed quite elevated death rates for lung cancer, varying from 7.6 through 9.8 to 20%. Combinations of four risk factors raised the death reate from lung cancer to 31%, demonstrating the strong synergistic effect of multiplying risk factors.

Of particular interest in this chapter is the group of 4 risk factor probands put in brackets; they had received prophylactic behaviour therapy (BT), and accordingly had a death rate from lung cancer only about 1/3rd as high as the group of 4 risk factor probands who received no therapy. Thus even for those most exposed to lung cancer prophylactic treatment is possible, and can be efficacious. A later chapter will deal with the prophylactic effects of behaviour therapy.

In another study, using 684 selected probands having various combinations of 0 to 7 risk factors (smoking, stress, genetics, bronchitis, use of depressive drugs, contact with automobile emissions, contact with asbestos). The results are shown in Fig. 6,

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for various combinations of these factors; again the synergistic or multiplicative nature of these risk factors in producing lung cancer will be clear.

Fig. 6 here.

These studies add to the earlier evidence (Grossarth-Maticek, 1980, 1989; Grossarth-Maticek, Eysenck & Vetter, 1988) and are indicative of synergistic action. This notion of multiple risk factors interacting in a synergistic fashion is crucial for a proper appraisal of methods of prevention for cancer and coronary heart disease. The failure of monocausal intervention efforts (McCormick and Skrabanek, 1988; Eysenck, 1986) is almost certainly due to concentration on single risk factors, like smoking, rather than a more wide ranging consideration of many different risk factors. As we have seen, psychosocial factors are of particular importance, and may present a more useful point of departure for prophylactic action. Support for this hypothesis is given in the next section.

It should not be assumed that the notion of synergistic action finds support only in the Grossarth-Maticek & Eysenck studies. In a recent paper Perkins (1989) has argued that: "Interactions among the major coronary heart disease risk factors of smoking, hypertension, and elevated cholesterol may contribute substantially to the p prediction of CHD risks over and above the sum of the independent risks due to their factors." (p.3.) He surveys results which show that "the interaction of smoking and cholesterol and of hypertension and cholesterol may each as much as double the risks of CHD which might be expected if these factors acted only additively." (p.3.) He also comments on "the strong possibility of an interaction between chronic psychosocial stress and elevated cholesterol." (p.3.) Other

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authors who have argued in favour of synergistic interaction effects are Kleinbaum et al. (1982), Rothman (1974), Rothman & Keller (1972), Kannel et al. (1986) and Saracci (1987); Perkins (1987) and Walker (1981) as well as Kooperman (1981) and Perkins (1985) have also added to the methodological analysis of synergistic effects.

An example will illustrate methods and results. Kannel et al. (1986) have reported data on over 300,000 white males selected for inclusion in the MRFIT study already mentioned. For men between 35 and 45 years of age, in the lowest quintile of diastolic blood pressure (<76 mm Hg), the six year risk of CHD mortality among non-smokers without elevated cholesterol (i.e. background risks) was 0.6/1,000, while the risks due to smoking alone was 1.0/1,000 and the risk for non-smokers with cholesterol in the highest quintile (above 2.44 mg/dl) was 2.0/1,000. If the effects of smoking and elevated cholesterol were only additive, the risk of those with both factors present would be 2.44/1,000, i.e. the background risk of 0.6, plus the risk attributable to smoking (0.4) and to cholesterol (1.4). The actual mortality rate for this subgroup, however, was 4.8/1,000, i.e. twice that expected on an additive model, indicating an excess risk of 100%!

This is clearly an important area of research, and the concepts involved may explain why single risk factors so often fail to give consistent positive results. It is certainly completely inadmissible to use simple univariate analyses for risk factor studies in epidemiology; multivariate analyses are an absolute must (Wilhelmsen, Wedel & Tibblin, 1973). Certainly smoking emerges as a risk factor in conjunction with other risk factors, rather than by itself. For this, as well as for other reasons already adumbrated, talk of smoking as "causing" cancer or CHD is scientifically meaningless.

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The established facts of synergistic interaction between risk factors also have profound consequences for prophylaxis and prevention generally (Perkins, 1989). The relative failure of quitting smoking to reduce cancer and CHD mortality may be due to the fact that such quitting would only have any pronounced effects in people with more than one risk factor present. For people with no other risk factors except smoking, quitting smoking would have no effect on mortality, and their inclusion in any study would disguise any impact that quitting smoking might have on mortality.

This certainly is the implication of the published data summarized above, and particularly of our Table 7. Quitting smoking in persons of Type 4 would only have a minimal effect, if any, on mortality.

For readers who would like to have some more detailed information on the Grossarth-Maticek personality types, an Appendix has been provided which lists the questions in a short version of the questionnaire which has been used in more recent studies (Grossarth-Maticek, Eysenck, 1990). In these later studies, 2 more types have been added to the 4 types already mentioned, Type 5 relating specifically to rheumatoid arthritis, as well as to cancer, and Type 6 to drug addiction. Type 5 is characterized by rational-antiemotional behaviour, and Type 6 by anti-social, psychopathic behaviour.

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(7) Intervention studies in cancer and coronary heart disease.

In the preceding section we have attempted to demonstrate that psychosocial factors like stress and personality are important risk factors in the causation of cancer and coronary heart disease, and that specific personality constellations, reacting to stress, are particularly cancer-prone and coronary heart disease-prone. These relationships, although much stronger than those linking smoking to cancer and coronary heart disease, are still only correlational, and it is well-known that correlations cannot be used directly to infer causation. The best way of indicating that the relations observed are indeed causal is by some intervention method which brings to bear an experimental paradigm on the problem in question. We have attempted to do this by using methods of behaviour therapy (Eysenck & Martin, 1987) in an attempt to alter the behaviour of the cancer-prone or the coronary heart disease-prone person in the direction of our healthy Type 4. In other words, we have attempted to increase autonomous behaviour, and reduce the proband's dependence on other people, or his/her acceptance of situations which lead to negative consequences. In this section we will give a brief discussion of the methods used, and then go on to an evaluation of the effects of using these methods in a prophylactic manner. (For a more general discussion of prophylactic methods, see Aeberhardt, 1989.)

The therapy developed by us contains many features which are familiar, such as Wolpe's method of desensitization, Lazarus's development of coping mechanisms, social skills training, and others. The method has been called 'Autonomy Training', or 'Creative Novation Behaviour Therapy'. The major aim of the treatment is to stimulate

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an individual to look towards the long-term positive results of different types of behaviour and self-evaluation (Grossarth-Maticek & Eysenck, in press). Thus it is the aim of the treatment to increase behaviours which lead to long-term positive consequences, even though this may involve some short-term negative consequences. Conversely, the patient should learn to avoid behaviours which lead to long-term negative consequences, even where these may be associated with short-term positive consequences.

Having briefly described the methods of prophylactic behaviour therapy, we must now consider their application to a variety of probands of Types 1 and 2, i.e. people prone to cancer and coronary heart disease respectively. Three major studies have been done by us, using respectively long-term individual therapy, group therapy, and bibliotherapy conjoined with short individual therapy. These studies will be discussed with respect to death, cause of death (as shown on the death certificate) and incidence, i.e. the diagnosis of cancer or coronary heart disease made by the patient's physician, and ascertained with the prior permission of the patient. All the studies were carried out in Heidelberg (West Germany), and the therapist in each case was Professor Grossarth-Maticek who originated the methods used.

Probands in the first of these studies, using long-term individual therapy, were 100 individuals, half male, half female, who were categorized as Type 1 (cancer-prone) on the basis of interview and questionnaire data. Their mean age was around 50 years. The second group of 92 individuals, similarly selected, but all of Type 2, were chosen to study the effects of behaviour therapy on coronary heart disease. The therapy consisted of roughly 30 hours of individual therapy, as outlined at the beginning of this chapter.

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The results are shown in Table 10. It will be seen that both for cancer and for coronary heart disease, the number of deaths is very significantly less for the therapy group than for the control group. The same is true for incidence which is roughly half in the therapy group as compared with the control group. These figures suggest very strongly that behaviour therapy can prevent death from cancer or coronary heart disease, or at least postpone it for a very considerable period of time. It is of course possible that the surviving members in the therapy group will ultimately die of cancer or coronary heart disease, or at least some of them will; only a much longer follow-up, until all the participants of the study are dead, can answer this question. What we do see is that 13 years after the initiation of the study, many more members of the therapy group are alive than of the control group.

Table 10 here.

It should also be noted that details of all probands were transmitted to two independent observers prior to ascertaining death and cause of death, or incidence, in each case. In addition, a random sample of interviewers was interviewed by an independent observer to check on the collection of interview and questionnaire data. These precautions were taken as a routine measure to certify the objectivity of the data collection.

Our second study is concerned with group behaviour therapy. In this case, groups of between 20 and 25 probands were formed, and administered group behaviour therapy for periods of between six and twenty-five hours, each group meeting lasting between two and three hours. Duration was determined by the members of the groups themselves, and hence varies to a considerable degree. Matching was

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carried out as before, and members of the group were followed up over an 8-year period. Results are given in Table 11.

Table 11 here.

It will be seen that group therapy, very much like long-term individual therapy, benefitted the therapy group, as compared with the control group, by reducing the mortality from cancer and coronary heart disease, and decreasing the incidence. Given the relative unreliability of diagnoses as recorded on death certificates, the most impressive figure perhaps is that of the proportion still living, which indicates the power of behaviour therapy to prevent cancer and coronary heart disease. Again the procedure, including all the death certificates, was checked by an independent observer.

Our third study was concerned with a special kind of bibliotherapy, which centred on a text entitled: "How to Achieve Emotional Independence and a Healthy Personality". This text was introduced to participants in an hour long introduction by Professor Grossarth-Maticek, who also outlined the application of the principles contained therein to the individual proband. After a week or so to give the proband time to read and understand the text, and try to apply it to his/her own condition, specially trained students went to discuss this application of the message contained in the text to the individual's circumstances, for three one-hour periods. What we are dealing with here, then, is not just bibliotherapy, but in addition some four hours of individual therapy.

In this study the therapy group was constituted of 600 probands, matched as before with a control group of 600. Again probands were allocated on a chance basis to therapy or control. Within the control group, a small group of 100 was exposed to a placebo

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treatment, i.e. using a psychoanalytic text outlining Freudian ideas concerning the origins and prevention of cancer. Table 12 shows the results of the study. It will be seen that the placebo group does not differ significantly from the control group, but the therapy group is superior to the control group both with respect to smaller number of deaths from cancer and coronary heart disease, and lower incidence of these two diseases. The data show that even a relatively short-term application of behaviour therapy, together with bibliotherapy, can have a marked effect on mortality and incidence of cancer and coronary heart disease.

Table 12 here.

More detailed information concerning these studies is given by Eysenck (1988a, b; 1989; Grossarth-Maticek, Bastiaans, and Kanazir, 1985; Grossarth-Maticek, Eysenck & Vetter, 1988; Grossarth-Maticek, Schmidt, Vetter & Arndt, 1984). These communications also contain information on the possibilities of prolonging life even after terminal cancer has been diagnosed. It seems that the use of behaviour therapy can delay deaths from cancer and almost double the duration of survival.

It is sometimes said that the results of behaviour therapy in cancer and CHD, either prophylactically or in prolonging life, are too good to be true, yet there is much outside evidence for the efficacy of different types of psychological therapy on cancer and CHD, some of which reports results even better than those described above. To take only the most recent study, Spiegel et al. (1989) was able to double the life expectancy of female patients with metastatic breast cancer, a result even better than similar studies reported by us (Eysenck,

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1988a, b). In Spiegel et al's control group, life expectancy was 18.9 months, while in the therapy group it was 36.8 months. Such findings should be seen in the context of studies looking at the influence which psychosocial factors and interventions have on the immune system, which presumably mediates the effects of life-events, stress and therapeutic psychological intervention, and the occurrence and rigour of cancer. Before turning to a consideration of this evidence, it may be useful to consider studies sugesting the possibility of prophylactic intervention in coronary heart disease-prone probands.

Johnston (1989) has reviewed the literature in a very critical spirit, but concludes that the evidence for the view that stress management may reduce coronary heart disease through the lowering of a large number of stress related risk factors by moderate, or even small, amounts "is patchy, but a much stronger case can be made than would have seemed possible only ten years ago". (p. 277.) The cautious optimism of this quotation is mainly based on the contributions of Friedman (1987), Friedman et al., (1984, 1986), Gillet et al. (1985), Lovibond et al. (1986), and Patel et al. (1985); most convincing are the data presented by the recurrent coronary prevention project. If the results are less striking than those reported by Grossarth-Maticek, Eysenck & Vetter (1988), this may be due to the fact that the validity of the Type A concept is probably much lower than that of the Grossarth-Maticek Type 2, i.e. the coronary heart disease-prone type (Booth-Kewley & Friedman, 1987). It is also noteworthy that the theory linking stress with cancer, and stress-reduction with cancer survival, has been elaborated much more convincingly (through the innervation of the immune system) than can be said of the relation between stress and stress management, and coronary heart disease.

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Bennett & Carroll (1990) similarly conclude a review of the evidence by saying that stress management techniques "not only reduce individual risk factors, they can also reduce mortality and morbidity to CHD." (p.1.) They also conclude that "risk factors combine multiplicatively, and small decreases on a number of risk factors may reduce the risk of CHD more than if only one risk factor is targeted (Johnson, 1989; Perkins, 1989), as in most medical interventions." (P.81.) These conclusions are very much in line with our own studies.

Finally, we may quote the conclusions drawn by Taylor (1990) in his review of Health Psychology: "Research that examines whether or not psychological and social factors are involved in health and illness has largely made its point..... Investigations have addressed the direct impact of stress and other psychological states on physiological processes, the impact of psychological and social factors on risky health practices, and the impact of psychological and social factors on how people respond to potential illness states, such as whether or not they engage in appropriate illness behaviour. As such, the field has advanced to an unprecedented level of complexity in research investigations... Health psychology affords the opportunity to look beyond particular disorders to the broad principles of thought and behaviour that cut across specializations of diseases or problems studied to elucidate more fundamental psychosocial mechanisms." (p.46.)

Some of the resulting complexities are illustrated in the work of Brown & McGill (1989) and Scheier et al. (1989). The importance of optimism in the recovery of patients from coronary artery disease by-pass surgery was highlighted by Scheier et al., demonstrating again the interaction of psychological states, personality and medical

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illness of recovery. Brown & McGill demonstrated the complex interaction of personality traits like optimism, which is closely linked with extraversion (Eysenck & Eysenck, 1985) and stress.

Positive life events are generally believed to have beneficial effects on health, but apparently this is only true when probands have a positive self-concept (optimism). Brown & McGill (1989) outline an identity disruption model of stress, which holds that an accumulation of life events that are inconsistent with the self-concept leads to illness. Thus positive life events in probands with a negative, pessimistic self-concept were predicted (and found) to predict the development of illness over time. Clearly, over-simplified concepts of "stress" may lead to erroneous predictions, and may account for many failures to replicate in the literature.

The findings of Brown & McGill find support in an experimental study by Brebner (1990) who showed that introverts tend to generalize experiences of failure, extraverts experiences of success, thus developing pessimistic or optimistic personality traits. Brebner considers such generalization of failure experiences as an important form of stress, but of course it is not usually mentioned in traditional stress inventories. It is noteworthy that the characteristics of cancer-prone probands agree to a considerable extent with those of introverts, while CHD probands tend to show more the characteristics of extraverts (Eysenck, 1990). These apparent relationships between predisposition to disease and well-established personality types are well worth following up along theoretical and experimental lines.

A brief outline may here be given of the way the connection between personality/stress and disease may be mediated by hormonal and physiological factors. A more detailed outline is given elsewhere

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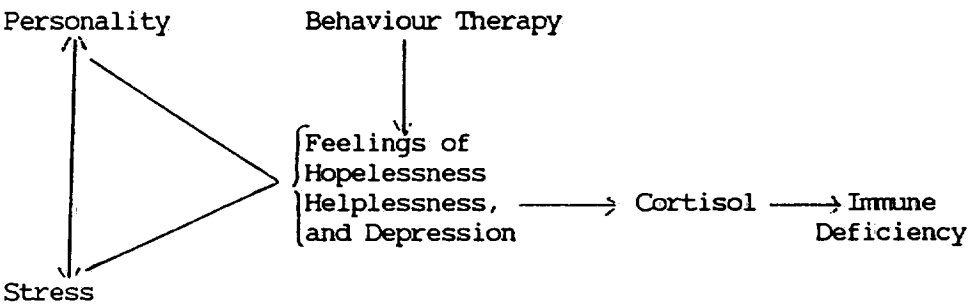
(Eysenck, 1986). The figure below illustrates the assumed causal pathway. Personality (Type 1) and stress combine and interact to produce feelings of helplessness, hopelessness and depression; these in turn produce hormonal and other reactions of which cortisol is here given as the representative (others are the endogenous opiates, ACTH, etc.). These in turn produce immune deficiency, which allows budding cancers to develop. The well-established fact that immune reactions can be conditioned along classical lines suggests one possible way such reactions may be learned. (Ader & Cohen, 1975; Solvason, Ghanta & Hiramoto), 1988.) There is a good deal of evidence to support such a model.



The model owes much to a similar one by Solomon (1987, in press; Solomon & Moos, 1964; Solomon, Levine & Kraft, 1968) who has argued powerfully for the concept of an "immunosuppression-prone" personality (Solomon, 1985). Having surveyed the literature, he produced first 35, and later another 30 postulates, many of which are relevant to our discussion. The main postulates of interest here are given below, numbered in sequence.

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Solomon's Postulates, 1987.

1. Enduring coping style and personality factors (trait characteristics) should influence the susceptibility of an individual's immune system to alteration by exongenous events, including reactions to events. (Thus, an "immunosuppression prone" behavioral pattern is hypothesized.)

2. Emotional upset and distress (state characteristics) should alter the incidence, severity, and/or course of diseases that are immunologically resisted (infectious and neoplastic) or are associated with aberrant immunologic function (allergic and autoimmune).

3. Severe emotional disturbance and mental dysfunction should be accompanied by immunologic abnormalities.

4. Experimental behavioral manipulation (for example, stress, conditioning) should have immunologic consequences.

5. Experimental manipulation of appropriate parts of the central nervous system should have immunologic consequences.

6. Hormones and other substances regulated or elaborated by the central nervous system should influence immune mechanisms.

7. Biochemical and functional similarities might be expected between the substances modulating the function and reactivity of the

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central nervous system (neuropeptides) and the substances with comparable effects on the immune system (cytokines).

8. Behavioral interventions (such as psychotherapy, relaxation techniques, imagery, biofeedback, and hypnosis) should be able to enhance or optimize immune function.

9. Altered CNS neurotransmitter receptor site sensitivities felt to be associated with mental illnesses should be reflected in lymphocyte receptors.

10. The "functional" modes of expression of CNS and immune system should be similar.

Linn, Linn & Jensen (1981) have shown that stress and anxiety are associated with depressed immunological response. Levy et al. (1985, 1987) found that natural killer (NK) cell activity in breast cancer patients was strongly correlated with psychosocial stress indicators which accounted for 51% of the baseline NK activity variance. Warburton & La Via (1987) found that tendency towards avoiding stress was the best predictor of immunocompetence. Green and Green (1987) reported that relaxation increases salivary immunoglobin A^1. Bandura et al. (1988) found that perceived self-inefficacy in exercising control over cognitive stressors activated endogenous opioid systems. Kiecolt-Glaser et al. (1984) found that distressed and lonely probands had significantly higher cortisol levels and a lower level of natural killer cell activity. Glaser et al. (1986) discovered stress-related impairments in cellular immunity, and Glaser & Kiecolt-Glaser (1985)

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